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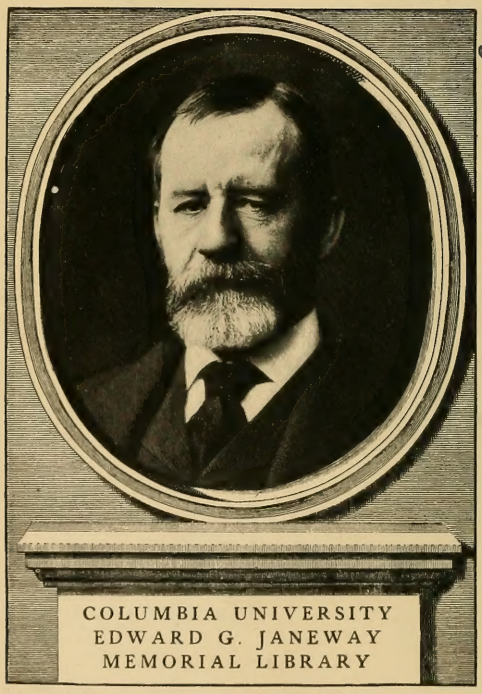

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INFECTIOUS DISEASES

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INFECTIOUS DISEASES

TYPHOID FEVER AND PARATYPHOID FEVERS

DYSENTERIES, CHOLERA AND EXANTHEMATIC TYPHUS

SYPHILIS AND THE ARMY

ABNORMAL FORMS OF TETANUS

MALARIA IN MACEDONIA

BY

H. VINCENT
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D. APPLETON AND COMPANY
NEW YORK AND LONDON
1918

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FOREWORD

The present conflict as viewed by the medical man emphasizes several outstanding facts. First among these is the fundamental truth that, despite the boundless variety of surgical injuries and the essentially specific internal medical diseases of warfare, the established principles of surgery and medicine still govern the art of the proper practice of these sciences. The application of these principles quite regularly demands modification in order to meet the changing conditions of warfare.

It is necessary, of course, that these modifications be adequately "proved out." The first step in this process of proving out consists in doing exactly what these volumes of the "Horizon Collection" seek to do,—namely, to present well coördinated data and conclusions to a broad and critical audience. The series of manuals really represents what Sir Alfred Keogh, in his foreword to Hull's *Surgery in War*, characterized as a "stock taking of the surgical position, to apportion value to various methods of treatment, and to obtain some appreciation of their results."

It is a privilege to be able to prophesy the service that these brochures will render to the Medical Corps of the United States Army in its efforts to emulate the zeal, resourcefulness and incomparable scientific enthusiasm of our allied professional brethren in France and England.

(Signed) W. C. Gorgas,
Surgeon General, U. S. A.

GENERAL INTRODUCTION

THE infinite variety of injuries which any war presents to the surgeon gives to military surgery a special interest and importance. The special interest and importance, in a surgical sense, of the great European War lies not so much in the fact that examples of every form of gross lesion of organs and limbs have been seen, for if we read the older writers we find little in the moderns that is new in this respect, but is to be found in the enormous mass of clinical material which has been presented to us and in the production of evidence sufficient to eliminate sources of error in determining important conclusions. For the first time also in any campaign the labours of the surgeon and the physician have had the aid of the bacteriologist, the pathologist, the physiologist and indeed of every form of scientific assistance in the solution of their respective problems. The clinician entered upon the great war armed with all the resources which the advances of fifty years had made available. If the surgical problems of modern war can be said not to differ sensibly from the campaigns of the past, the form in which they have been presented is certainly as different as are the methods of their solution. The achievements in the field of discovery of the chemist, the physicist and the biologist have given the military surgeon an advantage in diagnosis and treatment which was denied to his predecessors, and we are able to measure the effects of these advantages when we come to appraise the results which have been attained.

But although we may admit the general truth of these statements it would be wrong to assume that modern scientific knowledge was, on the outbreak of the war, immediately useful to those to whom the

wounded were to be confided. Fixed principles existed in all the sciences auxiliary to the work of the surgeon, but our scientific resources were not immediately available at the outset of the great campaign; scientific work bearing on wound problems had not been arranged in a manner adapted to the requirements, indeed the requirements were not fully foreseen; the workers in the various fields were isolated, or isolated themselves pursuing new researches rather than concentrating their powerful forces upon the one great quest.

However brilliant the triumphs of surgery may be, and that they have been of surpassing splendour no one will be found to deny, experiences of the war have already produced a mass of facts sufficient to suggest the complete remodelling of our methods of education and research.

The series of manuals, which it is my pleasant duty to introduce to English readers, consists of translations of the principal volumes of the "Horizon" Collection which has been appropriately named after the uniform of the French soldier.

The authors, who are all well-known specialists in the subjects which they represent, have given a concise but eminently readable account of the recent acquisitions to the medicine and surgery of war which had hitherto been disseminated in periodical literature.

No higher praise can be given to the Editors than to say that the clearness of exposition characteristic of the French original has not been lost in the rendering into English.

MEDICAL SERIES

The medical volumes which have been translated for this series may be divided into two main groups, the first dealing with certain epidemic diseases including syphilis, which are most liable to attack soldiers, and the second with various aspects of the neurology of war. The last word on *Typhoid Fever*, hitherto "the greatest scourge of armies in time of war," as it has been truly called, will be found in the mono-

graph by MM. Vincent and Muratet which contains a full account of recent progress in bacteriology and epidemiology as well as the clinical features of typhoid and paratyphoid fevers. The writers combat a belief in the comparatively harmless nature of paratyphoid and state that in the present war hæmorrhage and perforation have been as frequent in paratyphoid as in typhoid fever. In their chapter on diagnosis they show that the serum test is of no value in the case of those who have undergone anti-typhoid or anti-paratyphoid vaccination and that precise information can be gained by blood cultures only. The relative advantages of a restricted and liberal diet are discussed in the chapter on treatment, which also contains a description of serum-therapy and vaccine-therapy and the general management of the patient.

Considerable space is devoted to the important question of the carrier of infection. A special chapter is devoted to the prophylaxis of typhoid fever in the army. The work concludes with a chapter on preventive inoculation in which its value is conclusively proved by the statistics of all countries in which it has been employed.

MM. Vincent and Muratet have also contributed to the series a work on *Dysentery, Cholera and Typhus* which will be of special interest to those whose duties take them to the Eastern Mediterranean or Mesopotamia. The carrier problem in relation to dysentery and cholera is fully discussed, and special stress is laid on the epidemiological importance of mild or abortive cases of these two diseases.

In their monograph on *The Abnormal Forms of Tetanus*, MM. Courtois-Suffit and Giroux treat of those varieties of the disease in which the spasm is confined to a limited group of muscles, *e. g.* those of the head, or one or more limbs, or of the abdomino-thoracic muscles. The constitutional symptoms are less severe than in the generalised form of the disease, and the prognosis is more favourable.

The volume by Dr. G. Thibierge on *Syphilis in the*

Army is intended as a *vade-mecum* for medical officers in the army.

Turning now to the works of neurological interest, we have two volumes dealing with lesions of the peripheral nerves by Mme. Atanassio Benisty, who has been for several years assistant to Professor Pierre Marie at La Salpêtrière. The first volume contains an account of the anatomy and physiology of the peripheral nerves, together with the symptomatology of their lesions. The second volume is devoted to the prognosis and treatment of nerve lesions.

The monograph of MM. Babinski and Froment on *Hysteria or Pithiatism and Nervous Disorders of a Reflex Character* next claims attention. In the first part the old conception of hysteria, especially as it was built up by Charcot, is set forth, and is followed by a description of the modern conception of hysteria due to Babinski, who has suggested the substitution of the term "Pithiatism," *i. e.* a state curable by persuasion, for the old name hysteria. The second part deals with nervous disorders of a reflex character, consisting of contractures or paralysis following traumatism, which are frequently found in the neurology of war, and a variety of minor symptoms, such as muscular atrophy, exaggeration of the tendon reflexes, vasomotor, thermal and secretory changes, etc. An important section discusses the future of such men, especially as regards their disposal by medical boards.

An instructive companion volume to the above is to be found in the monograph of MM. Roussy and Lhermitte, which embodies a description of the psychoneuroses met with in war, starting with elementary motor disorders and concluding with the most complex represented by pure psychoses.

SURGICAL SERIES

When the present war began, surgeons, under the influence of the immortal work of Lister, had for more than a quarter of a century concerned themselves

almost exclusively with elaborations of technique designed to shorten the time occupied in or to improve the results obtained by the many complex operations that the genius of Lister had rendered possible. The good behaviour of the wound was taken for granted whenever it was made, as it nearly always was, through unbroken skin, and hence the study of the treatment of wounds had become largely restricted to the study of the aseptic variety. Septic wounds were rarely seen, and antiseptic surgery had been almost forgotten. Very few of those who were called upon to treat the wounded in the early autumn of 1914 were familiar with the treatment of grossly septic compound fractures and wounded joints, and none had any wide experience. To these men the conditions of the wounds came as a sinister and disheartening revelation. They were suddenly confronted with a state of affairs, as far as the physical conditions in the wounds were concerned, for which it was necessary to go back a hundred years or more to find a parallel.

Hence the early period of the war was one of earnest search after the correct principles that should be applied to the removal of the unusual difficulties with which surgeons and physicians were faced. It was necessary to discover where and why the treatment that sufficed for affections among the civil population failed when it was applied to military casualties, and then to originate adequate measures for the relief of the latter. For many reasons this was a slow and laborious process, in spite of the multitude of workers and the wealth of scientific resources at their disposal. The ruthlessness of war must necessarily hamper the work of the medical scientist in almost every direction except in that of providing him with an abundance of material upon which to work. It limits the opportunity for deliberate critical observation and comparison that is so essential to the formation of an accurate estimation of values; it often compels work to be done under such high pressure and such unfavourable conditions that it becomes of little value for educative purposes.

In all the armies, and on all the fronts, the pressure caused by the unprecedented number of casualties has necessitated rapid evacuation from the front along lines of communication, often of enormous length, and this means the transfer of cases through many hands, with its consequent division of responsibility, loss of continuity of treatment, and absence of prolonged observation by any one individual.

In addition to all this, it must be remembered that in this war the early conditions at the front were so uncertain that it was impossible to establish there the completely equipped scientific institutions for the treatment of the wounded that are now available under more assured circumstances, and that progress was thereby much hampered until definitive treatment could be undertaken at the early stage that is now possible.

But order has been steadily evolved out of chaos and many things are now being done at the front that would have been deemed impossible not many months ago. As general principles of treatment are established it is found practicable to give effect to them to their full logical extent, and though there are still many obscure points to be elucidated and many methods in use that still call for improvements, it is now safe to say that the position of the art of military medicine and surgery stands upon a sound foundation, and that its future may be regarded with confidence and sanguine expectation.

The views of great authorities who derive their knowledge from extensive first-hand practical experience gained in the field, cannot fail to serve as a most valuable asset to the less experienced, and must do much to enable them to derive the utmost value from the experience which will, in time, be theirs. The series covers the whole field of war surgery and medicine, and its predominating note is the exhaustive, practical and up-to-date manner in which it is handled. It is marked throughout not only by a wealth of detail, but by clearness of view and logical

sequence of thought. Its study will convince the reader that, great as have been the advances in all departments in the services during this war, the progress made in the medical branch may fairly challenge comparison with that in any other, and that not the least among the services rendered by our great Ally, France, to the common cause is this brilliant contribution to our professional knowledge.

A glance at the list of surgical works in the series will show how completely the ground has been covered. Appropriately enough, the series opens with the volume on *The Treatment of Infected Wounds*, by A. Carrel and G. Dehelly. This is a direct product of the war which, in the opinion of many, bids fair to become epoch-making in the treatment of septic wounds. It is peculiar to the war and derived directly from it, and the work upon which it is based is as fine an example of correlated work on the part of the chemist, the bacteriologist and the clinician as could well be wished for. This volume will show many for the first time what a precise and scientific method the "Carrel treatment" really is.

The two volumes by Prof. Leriche on *Fractures* contain the practical application of the views of the great Lyons school of surgeons with regard to the treatment of injuries of bones and joints. Supported as they are by an appeal to an abundant clinical experience, they cannot fail to interest English surgeons, and to prove of the greatest value. It is only necessary to say the *Wounds of the Abdomen* are dealt with by Dr. Abadie, *Wounds of the Vessels* by Prof. Sencert, *Wounds of the Skull and Brain* by MM. Chatelin and De Martel, and *Localisation and Extraction of Projectiles* by Prof. Ombrédanne and R. Ledoux-Lebard, to prove that the subjects have been allotted to very able and experienced exponents.

ALFRED KEOGH.

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BY

H. VINCENT AND L. MURATET

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SECTION I

TYPHOID FEVER AND PARATYPHOID FEVERS

TYPHOID FEVER AND PARATYPHOID FEVERS

FIRST PART

CLINICAL STUDY

Few diseases have benefited so much from laboratory research as typhoid fever. The discovery of the specific bacillus and of its presence in the blood before the appearance of the earliest symptoms, has modified our ideas of the etiology and pathogeny of this affection. The narrow limits within which it had been enclosed have been extended. We should no longer regard it as a purely intestinal affection as did Louis, Chomel, Trousseau, Bretonneau, Murchison, Grisolle, Jaccoud, etc. It represents the secondary localisation of a general affection produced by a specific bacillus. It is only a variety—the most frequent one, it is true—of typhoid septicæmia, "in the course of which disorders of the digestive system, important as they are, are far from representing the principal symptom of the disease" (H. Roger).

It is just this septicæmic character of typhoid fever which can explain the abundance of its symptoms. On a fairly uniform substratum of general and nervous clinical signs a great variety of morbid phenomena develops, which in turn are due to some remarkable localisation of the bacillus, *e. g.* meningitis, or to the predominance of one particular symptom or another, or to the insidious or unexpected development of a secondary infection, the clinical expression of which is

superimposed upon and confounded with the signs peculiar to typhoid fever.

We may add that it is above all others a disease full of surprises, and one in which sudden collapse of organic resistance occurs when it is least to be expected.

The result is that there is some difficulty in including in a single description a complete account of all the features of typhoid fever.

In our endeavour to succeed in giving as clear and complete a description as possible, the symptoms of typhoid fever have been discussed in this work according to the following plan.

The first chapter contains a comprehensive survey of the clinical characters of the most frequent form of typhoid fever.

The principal clinical types are then dealt with individually in a special study.

Finally, with the object of completing the necessarily succinct portions of the previous description, each of the principal symptoms and their varieties are discussed according to their anatomical localisation.

This last clinical chapter is, therefore, the necessary complement of the previous chapters.

CHAPTER I

CLINICAL CHARACTERS OF TYPHOID FEVER : ORDINARY FORMS

THE clinical forms of typhoid septicæmia with an intestinal localisation are multiple, but are only variants of one particular form, viz. typical typhoid fever of moderate intensity. From the clinical point of view we may adopt the division into four periods, *incubation, invasion or onset, height of the disease* and *defervescence.* This division is based on the course of the temperature, since it is the temperature which is the chief guide to treatment throughout the disease, and regulates the hygiene of convalescence. The temperature enables us to follow the course of the disease and frequently to foretell complications or improvement.

Incubation.—As a rule it is impossible to determine the onset of the infection and the time which elapses between this onset and the first symptoms. In the great majority of cases, however, the duration of the incubation of typhoid fever is fourteen, sixteen or twenty days.

Under certain circumstances the incubation period is much longer, and may last from twenty to forty days (Jaccoud, Apert).

In a case of laboratory infection, typhoid fever developed in forty days (Vincent).

Epidemiological observations also furnish numerous instances of long incubation periods. One may see cases of typhoid fever breaking out at intervals ranging from two to four or five weeks, without any intercurrent cause for infection having intervened.

This latent period of incubation is, as a rule, uneventful. No sign reveals the infection until the day when it is manifested by malaise, headache, digestive disturbance, and a rise of temperature with or without shivering. This combination of symptoms, however ill-developed they may be, should be looked on with suspicion, especially during an epidemic. In the course of the latent period of the disease a slight rise of temperature may be noted, the thermometer may register 99·0°, 99·4° or 99·8° F., either in the morning, which is rare, or at night, which is more frequent. In practice and in cases of possible infection these slight rises of temperature should be looked for methodically and systematically. They indicate the invasion of the organism by the typhoid bacillus, and *at this moment* it is possible to find the pathogenic microorganism in cultures of the blood.

Period of Invasion, or Onset.—In most cases the invasion takes place gradually, and the onset can only be determined retrospectively by questioning the patient.

The information so obtained is sometimes so indefinite that the doctor still feels in doubt, and has to reckon the onset of the disease from the day when the patient took to bed.

An individual who usually enjoys good health complains of having been out of sorts for several days. He feels tired and unsteady in his legs, he suffers from giddiness and tinnitus. His head feels heavy; all mental or physical exertion has become difficult, if not actually painful and distasteful. He is continually wanting to sleep, although at night his sleep is disturbed and he is constantly waking up. He has retained his clearness of mind and his memory, but when he speaks or answers questions put to him he does so with a certain effort. He complains of a slight pain in the lumbar region and his limbs. The appetite is lost, and there is a bitter taste in the mouth. The sight or smell of food sometimes causes nausea. The patient is constipated at first. The constipation is followed

by an ochre-coloured diarrhœa (four to five stools in the twenty-four hours), without colic. There is slight epistaxis. The urine is scanty. The skin is hot, the temperature is about 100·4° or 102·2°, the pulse quick, 110 to the minute. The features are drawn, the complexion slightly yellow, the cheeks red and the lips dry. The tongue is covered with a whitish coating and is red at the edges. The abdomen is slightly distended. On palpation one generally finds some tenderness and gurgling in the right iliac fossa. Pressure upon the epigastrium, as a rule, causes pain at the onset of the disease. The gall bladder is sometimes tender on pressure. Lastly, on auscultation of the chest one can often hear dry or moist sounds, indicating bronchitis.

Soon, however, the typical picture of enteric fever begins to appear.

The headache, which is chiefly frontal, gets more severe during the next few days. The patient feels giddy when he wants to raise his head or sit up in bed. He is restless in his sleep and suffers from nightmares. The spleen increases in size at the sixth or seventh day. Lastly, the temperature gradually rises. It goes up every evening without returning in the morning to the point at which it was on the previous morning. This is the period of ascending oscillations. The pulse does not keep parallel with the temperature, but is more rapid in the evening than in the morning, and becomes dicrotic.

Such is the ordinary clinical picture of the first period, which lasts from about four to seven days.

Height of the Disease.—In a second period which lasts on the average from a week to a fortnight, and sometimes more, the clinical picture becomes more definite. The temperature falls but slightly in the morning and keeps at about the level of 104° F. The pulse becomes frequent, soft and compressible. The headache diminishes, but the patient is prostrate and his facies becomes characteristic. During the daytime he is indifferent to persons and things, his intelligence appears less on the alert, he is slower in

replying and he is somnolent. But as soon as the evening comes he begins to be delirious, gets restless, has subsultus tendinum and carphology. After waking up in the morning he sinks back into the state of stupor (*τῦφος*), which has given its name to the disease. At the same time the tongue becomes dry and brownish at the base and centre, and increases in length, and the epithelial covering disappears at the tip and edges, which assume a glazed and red appearance, intersected by fissures which are sometimes quite deep.

The lips are dry and cracked, and the teeth covered with sordes. Throughout this period careful examination of the abdomen shows some small isolated spots, circular in shape, with definite outline, pink in colour, slightly round above the skin, disappearing for a moment on pressure, but soon reappearing. These lenticular pink spots are also present in very variable numbers on the chest and sides of the thorax.

One may also find ulcers present in the pharynx, the so-called Duguet's ulcers.

The skin is dry, but in the morning it is sticky and damp. Sometimes it is covered with "sudamina." The diarrhœa becomes more fœtid, the stools more frequent, the meteorism more pronounced; while the pain caused by pressure on the iliac fossa is severe enough to "cause the face of a comatose patient to contract" (Jaccoud).

The spleen grows larger and often passes below the false ribs.

The sphincters are sometimes relaxed, and the bladder is occasionally sluggish. The patient loses flesh considerably and gets weaker.

Death may occur in coma or the patient may gradually become convalescent.

Period of Defervescence.—The temperature falls either suddenly, which is rare, or rather slowly and gradually. In the first case "this sudden defervescence is complete in twelve hours, between the evening of one day and the morning of the next, or at the latest in thirty-six hours. The decline of the fever is accom-

panied by a complete change in the outward appearance of the patient : his facies becomes bright and assumes a normal expression. The organic recovery takes place quietly ; the phase of repair being reduced to a minimum and accomplished uneventfully, truly speaking, forms a part of convalescence " (Jaccoud).

In the second case, which is much more frequent, defervescence takes place gradually, by lysis. The temperature drops at first some tenths of a degree each evening, and then, having reached 101·8° or 102·2° in the evening, it falls to normal in the morning. This is the period of descending oscillations. The evening temperature also gradually becomes normal and remains so.

While the gradual fall of the temperature takes place in this manner, the patient comes to life again, as it were. The stupor disappears, the delirium subsides, the somnolence ceases, and he recovers consciousness of his condition and surroundings. The tongue, gums and lips become clear, the diarrhœa disappears, and very often gives way to constipation ; the meteorism diminishes, more urine is passed, the spleen resumes its normal dimensions, sleep returns, the appetite revives, and improvement takes place daily until recovery is complete.

Such in outline is the clinical picture of the typical form, and perhaps the most frequent form, of typhoid infection. This *ordinary form of typhoid fever* has special features which may be resumed as follows—

1. *Period of incubation* of varying length, usually two weeks, passing as a rule unnoticed, or brought into prominence by some malaise without specific character, and a very slight rise of temperature.

2. *Period of invasion or onset*, characterised by signs common to every infection : prostration, dizziness, vertigo, frontal headache, pains in the limbs and back ; coated tongue, sticky mouth, anorexia, nausea, occasionally vomiting, thirst, constipation, epistaxis, pain in the right iliac fossa, swelling of the spleen, and a special form of temperature (ascending oscillations).

3. *Height of the disease.*—Absolute anorexia, caked tongue, dry lips, pronounced meteorism, gurgling, diarrhœa and urine with special features, enlargement of the spleen, lenticular rose spots, typhoid state, delirium usually of slight degree, stupor, dicrotic pulse, temperature at a high level and excessive loss of flesh.

4. *Period of defervescence.*—Fall of temperature, sometimes sudden (rare), sometimes by lysis (descending oscillations), polyuria, return of appetite, and disappearance of the various symptoms.

But the disease is far from following step by step the schematic lines of this description, either at its onset or during its course. Sometimes one symptom or group of symptoms dominates the scene; sometimes the general course of the affection is prolonged or curtailed; and, lastly, the special features of an attack, according as it is mild or severe, have given rise to the description of numerous special forms.

From these forms we will select only those whose retention appears specially justifiable.

1. **Forms with Special Onset.**—*Sudden onset.*—Typhoid fever has not always a slow and progressive onset. There are cases where it "explodes," *i. e.* begins suddenly and with great violence. Trousseau and Murchison quote instances of the kind; Vincent has noted the special frequency of these forms in Algeria, among malaria patients.

The patients generally have a violent headache and a shivering attack, with a temperature about 104° F. In some cases there are pains in the joints, nausea and vomiting.

The serum reaction is positive earlier than usual (Widal).

Pneumo-typhoid.—In exceptional cases pneumonia may mark the onset of typhoid fever. The intensity of the pulmonary symptoms may cause one to overlook the signs of typhoid fever, which is recognised only at autopsy. Pneumonia and typhoid fever may be concurrent and both be diagnosed from the first. The pneumonia subsequently subsides and is replaced

by symptoms of typhoid fever, which then runs a normal course. This pneumo-typhoid is regarded by some authorities as the manifestation of the primary localisation of the typhoid bacillus (Gerhardt, Lépine, Grasset, Potain); according to others it is merely a superadded disease (de Marignac, Castex). Laboratory investigations have not yet cleared up this question.

Numerous clinical types have been created based on the predominance of an abnormal symptom, or on the more obvious localisation of the bacillus in a special organ at the onset of the disease.

Thus writers have described a *pleuro-typhoid*, in which the initial pleurisy precedes the manifestation of the signs of typhoid fever by eight to nine days; *arthro-typhoid*, *broncho-typhoid*, *meningo-typhoid*, etc. It would certainly be easy to add to these varieties.

2. Forms in which One or Several Symptoms Predominate.—Here, too, there has perhaps been a needless multiplication of symptomatic types.

The bilious or gastric form, with its bilious symptoms (nausea, bilious vomiting, slight jaundice) indicates the invasion of the bile ducts by the typhoid bacillus. It is frequent in hot climates, and has often been observed in the course of the present war.

Hæmorrhagic form.—All the principal infections may assume the hæmorrhagic form. Typhoid fever is no exception to this rule. In addition to the initial epistaxis, the mechanism of which is unexplained, and the hæmorrhage from the gums or mouth due to ulceration of the gums or mucous membrane, hæmorrhagic nephritis, due to typhoid infection, is also found. Lastly, intestinal hæmorrhage, which is more common, has a special pathogeny with which we shall deal later.

These hæmorrhagic forms may have an epidemic character (Leudet), which is perhaps explained by the activity of the toxins secreted by some strains of the typhoid bacillus.

These hæmorrhages may occur at any period of the disease, in any organ and in all parts of the body:

e. g. skin, mucous and serous membranes, intestine, uterus, lung, meninges, pleuræ, muscles, etc. The temperature is high, the heart fails and the patient is unable to offer any resistance. Death is very frequently the termination of these cases.

3. **Forms with a Shortened or Prolonged Course.**—*Abortive typhoid fever* (*typhus levissimus*). —Under this denomination are included "typhoid febricula of short duration, attenuated typhoid and certain cases of typhoid fever which are severe, but end in rapid recovery before the ordinary period of convalescence" (Letulle). They are fairly often seen in incompletely vaccinated subjects.

This abortive form of typhoid fever is specially found in children and is more frequent in certain epidemics (Letulle). At the onset the temperature may be very high, rising on the evening of the fourth or fifth day to 104° or 104·6° F., and associated with headache and complete insomnia; vomiting is not uncommon, the patient is usually constipated, there may be epistaxis. The rose spots appear from the seventh to the tenth day, but may be absent (Letulle).

The spleen is usually enlarged. The pulse is not very rapid, 70 to 90. The other symptoms are those of ordinary typhoid fever. The temperature may decline gradually to normal, or fall suddenly with copious perspiration. Critical polyuria may occur. These abortive fevers are frequently followed by relapses which are themselves often slight and abortive, but may be severe and fatal.

Prolonged typhoid fever.—In very exceptional cases typhoid fever is prolonged far beyond the ordinary limits. In one of Murchison's cases the appearance of rose spots was noted almost daily from the fourteenth to the sixtieth day. Typhoid fevers have been recorded which have lasted seventy and ninety days. In the so-called *recrudescing* forms the temperature shows a very slight fall, but soon returns to its former level, so that the duration of the disease may be thus considerably prolonged. In other cases the period of

defervescence is very long, but as a rule it is an exceptionally protracted amphibolic stage which prolongs the febrile period.

4. **Mild and Severe Forms.**—Typhoid fever presents all the intermediate degrees between apyrexia and hyperpyrexia; the temperature being as a rule the faithful expression of the severity of the disease.

Insidious or latent form.—Ambulatory form.—This form has been carefully studied by Louis, and Chomel and Louis. The expression, "ambulatory form," designates its special feature; the patient is up and about, and continues his ordinary occupation. In this form the symptoms are generally mild. The patient may have irregular shivers, alternating with flushes and feelings of heat, slight headache and lassitude; the appetite is lost, and sleep disturbed. There may be diarrhœa or constipation. The pulse is sometimes a little quickened, but may remain normal; rose spots may be found, as well as enlargement of the spleen. Fever may either be absent or very high (Jaccoud). Sometimes the ambulatory fever retains its character throughout and ends in recovery without the patient taking to bed. Sometimes towards the twelfth or fifteenth day the typical assemblage of typhoid symptoms appears. Lastly, in some cases the condition suddenly becomes alarming. The patient develops acute delirium or a sudden intestinal hæmorrhage, which may end fatally; or, more commonly, symptoms of perforation appear, with acute peritonitis, which is fatal in a few hours. Sometimes sudden death terminates what seemed to be quite a mild infection. The patient succumbs to myocarditis with stoppage of the heart. This cause of death has often been observed during the present war.

Febrile gastric derangement, synochus or typhoid febricula, belongs to the same clinical category as *typhus levissimus.*

This variety lasts seven to twelve days at most, and then the patient is quite well again. This febrile gastric derangement, which may also indicate a

paratyphoid infection, does not always run a mild course.

A blood-culture may confirm the diagnosis, as in certain so-called *apyretic* cases, in which the patient has no fever and complains only of vague discomfort and shows signs of anæmia and progressive weakness. This last form may be seen in enfeebled persons and subjects of chronic malaria.

Ataxo-adynamic or hyperpyretic form. — The old physicians used to differentiate between an *ataxic form* and an *adynamic form.*

In reality these two symptoms are as a rule associated, and are both accompanied by a high and prolonged temperature.

The ataxia is shown by more or less violent nervous disturbance: delirium, convulsions, subsultus, carphology, etc., alternating with adynamia, *i. e.* prostration, stupor and weakness of the voice. At the same time, feebleness of the pulse corresponding to the myocardial lesions becomes evident. The patient has frequent fluid stools, which are sometimes involuntary, and bedsores. The temperature ranges between 104·8° and 106·6° F., with very slight oscillations between the evening and morning records.

The ataxo-adynamic form with hyperpyrexia is extremely grave. Fulminating cases may occur which commence suddenly with violent headache and delirium, and terminate fatally in a few days.

Typhoid fever may assume special characters according to the state of the individual whom it attacks. The age, previous health, and co-existence of another infection profoundly modify the clinical characters of the disease. We will now study each of these modifications in turn.

Typhoid Fever according to Age

Typhoid Fever in Children. — (*a*) **Infancy.** — Typhoid fever in the infant is rather rare. At this age the diagnosis is peculiarly difficult. According to

Comby and Marfan, typhoid fever is exceptional in the first six months of life; from six months to two years its frequency increases.

Hutinel and Darré state that the principal cause of this immunity is the fact that the child does not leave the arms of its mother or nurse, and consequently is but little exposed to direct contagion. Its mode of feeding may also explain this rarity of infection. When typhoid fever does occur at this age, it is severe owing to pulmonary complications, especially secondary broncho-pneumonia of streptococcal nature, which is fairly often superimposed on the typhoid process.

In the case of a feverish infant one should first of all think of the eruptive fevers, and then of sore throat. The appearance and number of the stools, which are usually very liquid, fœtid, yellowish, sometimes greenish in colour, of porridgy consistence, and twelve to twenty-five a day; the acceleration of the pulse, *without dicrotism;* the appearance of rose spots combined with enlargement of the spleen; the state of prostration or, on the other hand, the infant's incessant cries and restlessness, are symptoms which should suggest typhoid fever. The serum reaction should be investigated.

Typhoid fever in the infant may assume one of three forms.

In the *gastro-intestinal form* the prostration is considerable; the little patient vomits its feeds and loses flesh considerably. The stools are numerous (six, twelve or twenty-five in the twenty-four hours), sometimes glairy (Nobécourt and Voisin). Green diarrhœa is fairly frequent and is accompanied by a high temperature. "This form is terribly fatal," says Marfan, "and as a rule in a few days' time a choleriform enteritis develops, probably due to a secondary infection, which carries off the patient."

In the *meningeal form* the clinical picture recalls that of meningitis: cries, restlessness, vomiting, very rapid pulse, fever without remission, constipation, a wild look, and strabismus. These phenomena of

excitement are succeeded by pronounced prostration. Trousseau's meningeal streak appears. Lumbar puncture gives issue to a fluid under tension, and causes a decided improvement in the little patient's condition. In other cases the reaction is intense; colic, shivering, vomiting, inequality of the pupils, ptosis, very pronounced internal strabismus, Cheyne-Stokes respiration, and death within ten days.

The least unfavourable variety is the so-called *febrile form.*

"A little diarrhœa, prostration, slight nervous phenomena, but nothing striking: the fever is the chief symptom" (Hutinel and Darré). The temperature curve sometimes resembles that of an adult, but as a rule it is rather irregular.

In favourable cases the fall of the temperature takes place slowly by lysis, occupying a whole week.

(*b*) **Childhood.**—Typhoid fever is fairly frequent in the child about seven or eight years of age, but is less severe than in the adult. The duration is also less, a fortnight only on the average, instead of a minimum of three weeks.

Abortive or curtailed forms are frequent.

The onset is often sudden, accompanied by vomiting lasting for twenty-four or forty-eight hours, or appendicular symptoms, or torticollis resembling rheumatic wry-neck. It may also simulate meningitis. In these cases the temperature goes up at once to about 104° F. These high temperatures of 104° and above have not the same severe prognosis as in the adult.

The pulse is relatively slow, 90 to 100 or 110 (Hutinel). According to Thoinot and Ribierre it is more rapid than in the adult (150–180 in very young children; 100–140 in older children).

Persistent constipation is almost the rule, followed by diarrhœa at a late stage. Meteorism is often ill-marked. In some exceptional cases, however, the belly is much distended, diarrhœa develops and becomes profuse. Enlargement of the spleen is almost constant.

Rose spots are more frequently absent in the child

than in the adult. They usually appear from the sixth to the twelfth day. They are sometimes particularly abundant and may become generalised (exanthematic form). The heart sounds may assume the embryocardiac rhythm, the extremities becoming cyanosed. Arteritis is infrequent; .phlebitis occurs fairly often. Hæmorrhages, though not harmless, are rarely fatal. Perforation occurs only in children of a certain age. It is manifested by a fall of temperature, abdominal distension, and later by porraceous vomiting. Colitis may mask the onset or occur in the course of typhoid fever. " In that case it is most frequently produced by enemata of boiled water which are not isotonic, and cause the passage of mucus and membrane into the stools. To make matters right again, enemata of mucilage are all that is required " (Hutinel).

In the course of typhoid fever in the child we may meet with meningeal reactions (meningism of Dupré), suppurative meningitis, pyelitis, and pyelonephritis; the last two complications supervening when the child has previously had a renal affection.

Albuminuria is frequent.

Aphasia of transient duration and without verbal deafness has been recorded.

Periostitis, especially of the tibia, is not rare. Otorrhœa is fairly frequent, causing deafness and often deaf-mutism in young children, who forget how to talk.

Besides desquamation and loss of hair, one may observe erythemata in young children, which indicate a severe infection. Such cases present ulceration and fissures of the lips, ulceration of the pharynx, and streptococcal ulceration of the skin. The patient is cyanosed, his temperature shows a sudden drop, the arterial pressure is low, the abdomen retracted, and he lies in a state of profound depression (Hutinel, Loiseau).

These are the grave forms which sometimes assume an epidemic character.

Generally speaking, with the exception of infants, typhoid fever in the child has a more favourable

prognosis than in the adult, and is especially favourable at about the age of ten or twelve years.

Typhoid in the Aged.—Although typhoid fever is rare above 40, fairly numerous examples are to be met with (61, 70, 73, 86, 90 and 100 in a case of Guéneau de Mussy). Its course is then abnormal and the prognosis extremely grave, doubtless on account of the visceral lesions of the heart, kidneys, lungs and arteries, which so frequently accompany old age. "The onset is usually insidious; debility and tremors are often prominent symptoms; the type of the fever is essentially adynamic. Rose spots, acute delirium and urgent diarrhœa are rarely observed. The pyrexia is usually protracted, but the temperature, even in fatal cases, is rarely so high as in younger persons, and more often falls below normal" (Murchison). We may add that pulmonary phenomena play an important part and are frequently responsible for the fatal termination.

Convalescence is always protracted, owing to gastro-intestinal troubles and mental disturbances, such as loss of memory, which is often permanent, or cardiac disorder which fairly frequently terminates by collapse.

Typhoid Fever in Pregnancy.—Pregnancy in itself is not an aggravating factor in typhoid fever. But the disease may, by its effect on the fœtus, cause abortion or premature delivery in about one out of three cases. Advanced pregnancy particularly predisposes to abortion, which may occur at any period of the disease, from the first week till the first days of convalescence (Hutinel).

In the great majority of cases the fœtus is expelled dead; when the child is alive its blood presents agglutinating properties (Widal and Sicard). Death of the fœtus has been attributed to profuse hæmorrhage from the endometrium or to hyperthermia, although this suggestion has not been confirmed.

The presence of specific agglutinins or of the actual typhoid bacillus in the blood (Chantemesse and Widal, Legry, Étienne, Marfan, etc.) or organs of the expelled fœtus, suggests that the fœtus may succumb to the

direct action of the infection transmitted to it by the mother.

Typhoid Fever in the Course of Various Pathological Conditions.—Certain persons who are already suffering from an acute or chronic disease may contract typhoid fever, or an acute infection may be grafted upon an already existing typhoid fever. This combination gives rise to the following interesting clinical forms.

Typhoid fever and acute exanthemata.—Murchison has recorded a case in which typhoid fever was complicated by *variola* and *vaccinia.* Barthez and Rilliet, Taupin, Jenner and Kesteven have seen cases of co-existent typhoid fever and *measles.*

Scarlatina has often been noted in typhoid fever. Usually the patient suffering from typhoid fever is admitted to hospital, where he contracts scarlatina. In a certain number of hospitals, both for children and adults, all diseases are treated in the same ward.

Typhoid fever and diphtheria.—In children's hospitals an attack of faucial diphtheria in typhoid fever may prove fatal in forty-eight hours. The association of diphtheria and typhoid fever often has a grave prognosis in the adult also.

E. Rathery has recorded an epidemic of typho-diphtheria in the army, in which the asthenic cardio-bulbar forms were remarkably frequent. Side by side with these forms there were others, dyspnœic forms of an asphyxial type, as well as laryngeal, broncho-pulmonary and nervous forms of a meningeal type. Rathery regards the peculiar dry state of the mouth in typhoid patients as likely to exalt the virulence of the diphtheria bacillus in the highest degree. Marcel Labbé, who saw nine cases in a month, states that the association of typhoid and diphtheria is shown by an aggravation of the general symptoms, a persistently high temperature, weakness of the heart, a small and feeble pulse, diminution of the urine and coldness of the extremities.

Typhoid fever and tuberculosis.—A tuberculous

patient may contract typhoid fever which develops normally, but in convalescence the tuberculosis may take on a rapid course. It is not exceptional to see a convalescent from typhoid develop undoubted signs of tuberculosis, and even of acute phthisis.

Erysipelas is a grave complication of typhoid fever, but has become rare since more care has been given to the lesions of the skin which are so frequent in typhoid patients.

The occurrence of streptococcal infection, at the onset or in the course of typhoid fever, has formed the object of a special study (H. Vincent), owing to the gravity of its prognosis.

When the streptococcal infection occurs in the first stage of typhoid fever, it may be the cause of disease without any affection of Peyer's patches. The patient succumbs to a veritable *strepto-typhoid septicæmia*, his blood containing an abundance of both micro-organisms. When it appears in the course of typhoid fever, it is much less severe.

Pneumonia may occur during typhoid fever; the pneumococcus is present in the sputum. It may be carried to the meninges and determine an extremely acute meningitis, or an exudative meningitis with a pseudo-membranous investment in which the pneumococcus will also be found.

The *bacillus pyocyaneus* and *proteus vulgaris* may, by secondary infection, invade the blood or viscera of the typhoid patient, but these complications are very rare (H. Vincent).

Cases of cholera (Girode) and tetanus (Rouget) in typhoid fever have been recorded.

In *alcoholic* patients typhoid fever assumes a severe character. At the onset the symptoms are those of an ataxo-adynamic fever without the hyperthermia being excessive. The principal symptoms are delirium, cardiac paresis and ataxia. Hæmorrhages and bed-sores are frequent.

In *diabetic* patients typhoid fever often runs its course without causing much disturbance; the tem-

perature is little raised, and the disease may be mild and almost latent. The glycosuria persists, and the diabetes is in no way modified in its character or evolution.

Typhoid fever is a serious complication in *cardiac*

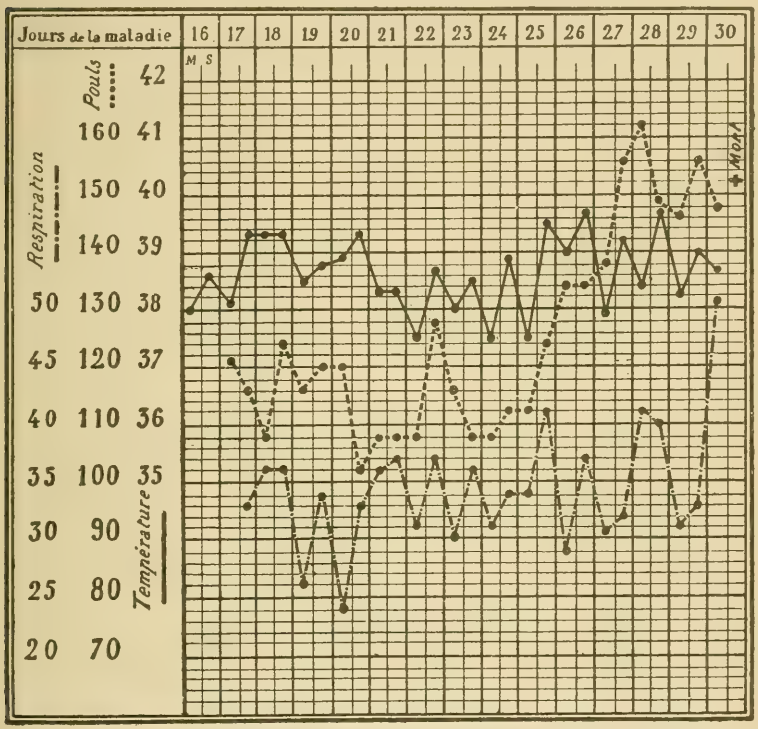


FIG. 1.—Typho-malarial fever. Unusual acceleration of pulse (140–162) after 25th day, myocarditis with embryocardia and death.

and *pulmonary* diseases, the pre-existing lesions being aggravated by the new infection.

Influenza fairly frequently precedes typhoid fever. Potain has drawn attention to the mild character of this post-influenzal fever, whereas Siredey, on the other hand, has seen severe and fatal cases under the same conditions.

Lastly, Kelsch and Kiener and Vincent have

described, under the name of typho-malaria, the association of malaria and typhoid fever in the same individual. (Fig. 1).

In malarial patients the onset of typhoid fever is often sudden, being characterised by a frank attack in the form of a quotidian fever with shivering. But the fever very rapidly becomes continuous. The ordinary severe typhoid symptoms then develop, especially if the malaria is not treated, viz. profuse diarrhœa, lenticular rose spots, meteorism, enlargement of the spleen and adynamic nervous troubles; while the malaria is revealed by enlargement of the liver, the earthy complexion and the periodic or irregular temperature. Sometimes pernicious attacks occur during convalescence and prove fatal.

As regards skin affections (eczema, scabies, hard chancres, etc.) they are only temporarily modified by the typhoid process.

Termination of Typhoid Fever

Death may occur at various periods of the disease, but rarely before the fourteenth day.

In hot countries, and also in overwrought soldiers, in war time, it is not exceptional to meet with death on the eighth and even on the sixth day of the disease, death being due to the hypertoxic forms.

Death may be the consequence of the severity of the infection; of localised complications, such as peritonitis, intestinal perforation, rupture of the gall-bladder, intestinal hæmorrhage, myocarditis, nephritis, etc.; of superadded infections, such as streptococcal or staphylococcal septicæmia, pneumonia, broncho-pneumonia, diphtheria, etc.

It may occur suddenly without a cry, a movement or a complaint of any kind. This sudden death, which is not uncommon (1 to 3 per cent. of the cases) most frequently takes place in the third week. It has been attributed to various causes, *e. g.* an intestinal reflex (Dieulafoy), degeneration of the myocardium

(Hayem), cardiac thrombosis (Marvaud), cerebral anæmia (Huchard, Laveran), pulmonary embolism, neuritis of the cardiac plexus, profuse intestinal hæmorrhage, etc. Myocarditis seems to have been one of the most frequent causes of rapid or sudden death in the present war. During the Tunis expedition one typhoid patient out of six succumbed suddenly (Czernicki).

The percentage mortality varies and is subordinate to the age, sex, nature of the treatment, degree of gravity of certain epidemics, climate and previous condition of fatigue or overwork.

In childhood the mortality is only 3 to 5 per cent., sometimes it is lower still. In the adult the average is 11 to 14 per cent.

In the aged the course of the disease is more rapid, and death is very common. The mortality in women is lower than in men.

The rational employment of cold baths has appreciably diminished the gravity of the infection, and the number of deaths. Some epidemics, however, are remarkable for a high mortality, and others for their milder character, which indicates the varying pathogenic power of the different strains of the typhoid bacillus, as is the case with the bacilli of dysentery, cholera, etc. In hot countries the case mortality is considerably higher than in cold or temperate climates, either because the external temperature adds its own influence to that of the fever, or because the micro-organisms are more toxic.

Lastly, in patients in broken-down health, or who have come under treatment late, or who have been overworked, the mortality may be as high as 20 and even 25 per cent. The state of war greatly predisposes to a grave prognosis in combatant soldiers, among whom the mortality is very high.

Recovery only takes place after a more or less protracted period of *convalescence*, which may be normal or *complicated.*

" Convalescence can only be said to be fairly estab-

lished when the temperature is normal on two successive evenings " (Murchison). But it is still very unstable. By the time convalescence begins the patient has become very thin, the loss of weight sometimes amounting in the course of the disease to 200–300 grammes per day, and even more. His skin is of a peculiar colour : " he has the face of a starved man " (Hutinel). His cheeks, hitherto coloured by fever, become decidedly pale. His pulse is irregular, is quickened by the slightest effort, an insignificant emotion, or the doctor's visit. The appetite returns, however, and is truly ravenous. The urine, after the transient polyuria and chloride discharge, becomes normal again in quantity, and poor in chlorides and urea. The muscular system is weakened, walking and standing are difficult and painful, the patient is quickly tired but recovers his strength gradually. The skin peels, the nails present furrows and depressions, the hair falls out but grows again as repair takes place, the weight increases and the anæmia disappears.

Some convalescents will be found to have lost their memory and present disturbances of hearing, taste and smell; they are very impressionable, and sometimes show temporary modifications in their character (excessive apathy, starvation delirium or irritability). As a rule, however, the disappearance of fever is accompanied by a marked sense of well-being.

The duration of convalescence varies considerably, being more rapid in children and longer in adults above forty years of age.

There are few cases of typhoid fever in which the disease or convalescence is not interrupted either by some slight incident or grave complication.

Typhoid fever is pre-eminently a disease with complications.

Venous thrombosis is a fairly common occurrence in convalescence, being due to the growth of the staphylococcus, and in exceptional cases of the streptococcus, in which case the prognosis is very grave. Typhoid arteritis is rarer. Convalescents sometimes

suffer from obstinate vomiting, which may become uncontrollable and even be the cause of death.

Cachectic diarrhœa may persist indefinitely and considerably weaken the patient. Paralysis from neuritis, abscesses and boils are not rare. Some convalescents may show œdema without albuminuria, which clears up in two or three weeks, and the pathogeny of which is still obscure. After long and severe illnesses bedsores may be the starting-point of septicæmia, which is sometimes fatal. The temperature *ought* to be normal in convalescence, but the thermometer may rise for some hours under the influence of fatigue, emotion, excess of food or a meat diet (*febris carnis*).

When the rise of temperature lasts for more than a day it becomes the first symptom either of an intercurrent complication (phlegmasia alba dolens, osteitis, various suppurative lesions, etc.) or of the interruption of convalescence by a relapse.

Relapses

By a relapse of typhoid fever should be understood a second evolution of the specific febrile process after convalescence from the first attack is fairly established. Relapses should not be confounded with recrudescences, which are common during the period of ulceration, nor with second attacks.

Recrudescences are aggravations of the typhoid symptoms which usually occur in the period of defervescence. The disease " rebounds," so to speak, and when it appears to be on the way to convalescence, it breaks out again.

A *relapse* is a revival of typhoid fever in actual convalescence; that is to say, when the patient has had a normal temperature for several days.

The *second attack* is a fresh attack of typhoid fever occurring a very long time after recovery from the first. Although as a rule the first attack confers immunity, this immunity may be attenuated or lost

after a varying period of time, thus rendering possible a fresh typhoid infection.

The relapse begins from eight to thirty days after the termination of the febrile cycle (Jaccoud); as a rule, however, it does not develop after the end of the first fortnight. It may start after an apyrexial period of from one to three days.

It reproduces completely and in their normal order all the symptoms of typhoid fever.

The first symptom is the rise of temperature, which may occur just as at the onset of typhoid fever, viz. either suddenly or by more or less pronounced ascending oscillations, with or without shivering. The ordinary symptoms reappear. The eruption of rose spots appears earlier than in the first attack.

The duration of the second attack is usually, but not invariably, shorter than that of the first. As a rule, the relapse is fairly mild. The severity of the relapse has no relation to that of the initial disease. In a third or quarter of the cases the symptoms are severer than in the first attack. The relapse is not always single. Cases of typhoid fever with multiple relapses have been seen, *e. g.* two (Trousseau, Stewart, Maclagan), three (Bucquoy, Jaccoud, etc.), four (Hallopeau), and even five relapses (Jaccoud). Perhaps the last was a case of Malta fever.

Sequelæ of Typhoid Fever

In the majority of cases recovery from typhoid fever takes place without any sequelæ.

Typhoid fever may, however, leave behind lasting traces of its visit in the form of disablement and chronic visceral lesions, or pathological states which appear during the fever and continue their course after the fever has ended.

Writers have recorded cases of prolonged and even permanent enfeeblement of the memory, slowness of perception, difficulty in the formation of ideas, disturbance of speech, and in children and young persons

" a lowering of the intelligence, which increases through want of exercise, and may end in a condition bordering on imbecility " (Jaccoud).

Acute mania, melancholia, megalomania, religious mania, etc., have been observed as the results of typhoid fever.

Polyneuritis, disseminated sclerosis, chorea and anterior poliomyelitis have been recorded.

Nephritis is rather rare; paratyphoid appendicitis has been described by Dieulafoy.

Prolonged infections of the bile ducts, and some forms of biliary cirrhosis may be attributed to a previous typhoid infection, owing to growth of the bacillus in the gall-bladder and bile ducts.

There are many cases on record of osseous and articular lesions, such as hip-joint disease and coxo-femoral dislocation, as well as mutilations of the extremities following gangrene due to arterial obliteration. Lastly, in the antecedents of patients suffering from leukæmia, Hodgkin's disease (Reynaud), and splenic pseudo-leukæmia, typhoid fever has been noted, without, however, any demonstration of the relation of cause and effect between these diseases and the typhoid infection.

CHAPTER II

CLINICAL CHARACTERS OF TYPHOID FEVER
(*continued*).

Analysis of Symptoms and Complications according to their Anatomical Situation

Digestive System

The symptoms presented by the digestive organs in typhoid fever are most important. Except in the mild cases, where the patient preserves it throughout the disease, the *appetite* is already declining in the incubation period and is completely lost at the height of the disease, to reappear again in the course of defervescence, when its demands are imperious and dangerous.

According to Vaquez, the anorexia is mainly due to the insufficient diet to which the patients are restricted.

Thirst is complained of. There is a bitter taste in the mouth. The salivary secretion is diminished. The restricted diet, fever and *diarrhœa* are factors in the diminution of these secretions. P. Merklen and Milhit, however, have reported a case of abundant ptyalism followed by sialorrhœa, with painless bilateral parotid and submaxillary swelling.

At the onset and during the first few days of the disease the tongue may be broad and flabby, and show the marks of the teeth at its edges. It soon becomes narrow, tapering and more or less pointed. The epithelial covering disappears at the tip and edges, so that the central part, which remains white or yellowish white, is surrounded by a bright red zone placed like an isosceles triangle with its base posteriorly. In

other cases, on the contrary, the coating disappears from the centre of the organ, which then projects like a red V into the middle of the white zone (Jaccoud). When the course of the disease is normal, and devoid of gravity, the tongue retains this appearance. When the disease lasts longer and assumes a more severe form, the redness of the tip and edges becomes more marked, a red punctation appears at these points and the central coating gets thicker. Lastly, in the grave forms with a severe "typhoid state," the tongue gets dry and assumes an appearance which has given it the name of "roasted tongue," "grilled tongue," or "parrot's tongue." It becomes retracted, hardened and shrivelled, its movements are difficult, uncertain and painful. Its thick coating becomes brown or blackish, crusted and cracked; it is formed by dried epithelial cells and mucus, and coloured by the blood which has oozed from the cracks. The lips become dry, cracked and covered with sordes. When the typhoid state is established the teeth become covered with a similar coating. In very rare cases the gums are the seat of hæmorrhage.

The soft palate, uvula, tonsils and pharynx take on a red tint and become covered with a brown coat.

In severe attacks various forms of sore throat are seen as complications, such as tonsillitis, diphtheria and gangrenous angina.

Thrush is fairly often observed. It appears on the soft palate, sometimes on the back of the pharynx, almost always on the pillars and tonsils, rarely on the cheeks and tongue, and hardly ever on the gums and lips; sometimes it covers the uvula, and is accompanied by extreme dysphagia. It yields to treatment, but recurs with an exasperating obstinacy.

R. Tripier, Devic, Johanno, Letulle and others have dwelt on the appearance of bucco-pharyngeal *ulcerations* in typhoid fever. These isolated or multiple ulcerations, apparently due to local infection by the pathogenic flora of the mouth, may be found on the tongue, lips and cheeks, soft palate, uvula, in the

gingivo-labial fold and at the frænum, and, in exceptional cases, on the posterior pillars.

In addition to these ulcerations there are others, noted for the first time by Bouveret in 1876 and called "Duguet's ulcerations." They are to be seen in one out of five cases. They really constitute a symptom and not a complication of typhoid fever. Their seat of predilection is on the anterior pillars of the palate.

They are fairly often situated symmetrically on the two palatal pillars, where they appear in the form of a whitish or ashy grey patch, slightly oval in shape, running obliquely downwards and outwards, with their long axis parallel to that of the corresponding pillar, and measure six to eight mm. in diameter. On their surface is to be found a little mucus, which is easily removed, leaving an almost normal mucous membrane which does not bleed, is not indurated, and is of a yellowish grey or grey pink colour. The ulceration is shallow, its edges are regular and surrounded with a small red area of congestion.

On the edges of the tongue may be seen ulcers of a different appearance, as they are deeper and their edges are sharply cut. The mucous membrane surrounding them is swollen and bleeds readily. They are specially situated at points which are subject to pressure or the action of the teeth, whether in the dorsal or lateral decubitus.

They are kept up by the dryness of the mouth and prolonged immobilisation resulting from the rarity of movements of mastication and deglutition, and lastly by the local infection caused by the microbial flora of the buccal cavity. They are absolutely painless, have hardly any effect on the neighbouring lymph glands, and are most frequently met with in severe forms of typhoid fever.

The ulceration of the palatal pillars appears before the beginning of the second week, at the same period as the lenticular rose spots.

They are characteristic enough to confirm a diagnosis of typhoid fever.

Very rare cases occur in which, apart from the fever, the only symptom referable to the digestive tract has been this ulceration of the pillars, the patients having had no meteorism, diarrhœa or nervous symptoms. As they generally disappear at the same time as the fever, they serve to a certain extent as a guide to the course of the disease. Their persistence may herald a relapse ; while their disappearance, even if it does not eliminate the possibility of a relapse, is of favourable prognosis, the relapse being usually mild (Devic).

The practical importance of looking for these ulcers is obvious, possessing as they do the value of a specific sign, with the exception of the lingual ulcers, which have been noted in other acute diseases.

Louis has described pharyngeal ulcers which appear late (third or fourth week); they are multiple and deep, and situated at the lower part and sides of the pharynx, where they cannot be seen by the unaided eye. Their course is generally insidious, but they may be the starting-point of more serious complications, especially retro-tonsillar or retro-pharyngeal abscesses. They may also cause œdema of the glottis.

Gastric Symptoms.—Pain and tenderness on pressure on the epigastrium are very frequent, especially at the onset. They may or may not be accompanied by vomiting.

It is also at the onset of typhoid fever that vomiting is observed in the adult, and still more frequently in children.

It is caused by a feed or a dose of medicine. As a rule the patients have a sense of fulness and tension, with nausea and distaste for food. At the height of the disease uncontrollable vomiting may be caused by the absorption of very small quantities of fluid, and may even be complicated by hæmatemesis.

When it occurs in convalescence, vomiting may merely be a sign of indigestion, or herald a relapse. It is rarer in patients who have not been subjected to a rigorous diet throughout the febrile period (Jaccoud). The best treatment at this time is to give them solid

food (Trousseau). Less frequently the vomiting is due to ulcerative lesions of the stomach and degeneration of the glandular cells of the epithelium, which have not retained, or have been unable to recover, the integrity of their functions.

Intestinal Symptoms.—Abdominal pain and tenderness are frequent but not constant symptoms. They are rarely spontaneous; pressure over most of the intestine is painless, but on the right iliac fossa it causes almost always a characteristic pain, sometimes severe enough to provoke a grimace, a cry or a movement of defence on the part of the patient, however prostrate he may be. This symptom is a more or less early one; it may persist until convalescence, or reappear at that period as the result of constipation or an error of diet. The pain may be found especially at MacBurney's point, and reveals the share taken by the ileum and appendix in the localisation of the infective process.

Meteorism is almost constant. It may be present from the onset, but as a rule it is not definitely appreciable before the end of the first week, and becomes marked in the course of the second. When the intestine contains only a little gas, the abdomen assumes a special shape. It is distended transversely. The umbilicus is very often seen to project. The consistency is elastic on palpation; the resonance of the abdomen is exaggerated on percussion. In extreme cases, with an enormous quantity of gas in the intestine, the intestinal distension becomes generalised, the thorax becomes broadened at the base, the respiratory action of the diaphragm is interfered with, and a more or less serious pulmonary stasis ensues. The frequency and intensity of the meteorism are related to the gravity of the disease (Jenner, Louis, Murchison).

Gurgling.—In a large number of cases a more or less marked gurgling is observed when pressure is made abruptly in the right iliac region. This examination should be made with great care, for any injury to a distended and ulcerated intestine should be avoided.

A good and prudent method of investigating the presence of gurgling is to employ bimanual palpation, using each hand in turn.

According to Jaccoud, gurgling merely indicates that the patient has, or has just had, diarrhœa. It possesses diagnostic value only when it is accompanied by other specific symptoms, and if the patient has no diarrhœa, and has not been given an enema or a purgative.

"Diarrhœa is the rule in enteric fever and constipation the exception." Murchison's formula is perhaps too absolute. Although one may have observed certain cases of an ambulatory type in which the patients complained of diarrhœa only, the date of appearance and duration of the diarrhœa are so variable that this symptom is of little help in diagnosis. It serves, however, to confirm the diagnosis in certain cases by the special characters which it presents.

The diarrhœic stools in typhoid fever are liquid and of yellow ochre or melon-juice colour. They leave a yellowish stain on the sheets, surrounded by a broad zone of a faint pink colour. Their reaction is alkaline, their odour sometimes fœtid and sometimes musty. On standing they leave a flaky sediment, and may contain blood. Their evacuation is not accompanied by colic or tenesmus.

Diarrhœa may be present from the onset of the disease, but usually the patient is constipated. After a purgative the stools are mashy and unformed, and rapidly become liquid. Their frequency is very variable according to the patient. Usually they are not very numerous at the onset (three or four in the twenty-four hours), and the maximum number is reached towards the middle or end of the second week, when they may amount to ten, twelve or twenty in the twenty-four hours. In such cases, which indicate the severity of the infection and are related to the gravity of the disease, the diarrhœa may become an actual danger owing to the amount of water which it removes from the system. The patient's face grows pale, his

features are drawn, his skin grows dry, his peripheral temperature falls, his pulse becomes frequent and small, and collapse may ensue. The discharge of fæces may be involuntary, indicating a profound state of prostration, and causing an erythema of the buttocks and over the sacrum.

The diarrhœa usually disappears at the end of the fastigium or at the beginning of convalescence. It is not exceptional, however, to see it cease rapidly and be replaced by an obstinate constipation, which lasts until the end of the fastigium. Then, as a rule, the diarrhœa returns, and sometimes continues till the end of convalescence.

In very rare cases constipation is more persistent and lasts throughout the disease.

Intestinal hæmorrhage.—Intestinal hæmorrhage is an important symptom. It may be one of the *early* signs of a special form of typhoid fever called *hæmorrhagic*. It is then of a severe prognosis. Sometimes it is slight and appears towards the tenth or twelfth day of disease. But more frequently it results from the opening of an arteriole in an ulcer or erosion of a vessel by separation of a slough, in which case it occurs towards the fifteenth or twentieth day. It may be later (thirty-third, forty-fourth, forty-ninth day). It is rare in the child, uncommon in the adolescent (twelve to fifteen years), and is more frequent in the adult and in certain epidemics. Diabetes preceding typhoid fever seems to predispose to hæmorrhage, owing to the arterial hypertension which is the rule in diabetes (Teissier).

Late hæmorrhage, especially that occurring at the end of the third week, appears with equal frequency among patients with diarrhœa or constipation. The quantity of blood lost may vary from a few drops to several litres. Sometimes the intestinal hæmorrhage is fulminating, and causes death before blood has appeared in the stools.

In such cases one may be guided by a sudden fall of temperature, a syncopal attack, an almost instan-

taneous decrease in the size of the spleen, a transient rise of the blood-pressure (Teissier), an increase in frequency of the pulse (Trousseau), and a disappearance of dicrotism of the pulse (Bouchard).

But as a rule the blood appears externally. When it is scanty, microscopical examination is necessary to reveal it. Spectroscopical examination must also be employed when this method is possible. The phenolphthalein reaction (Meyer's reaction) is too uncertain, and should not be recommended (Hugounencq-Labat). The same applies to the reactions with benzidine and tincture of guiacum.

The blood often appears in the form of red streaks. When present in larger quantity, it gives the stools the crimson appearance of normal blood; or, if it has been some time in the intestine, its colour changes to that of sepia, pitch or tar.

The general symptoms of intestinal hæmorrhage vary considerably, according to the quantity of blood lost. In the case of small hæmorrhages there are no symptoms.

When the loss of blood is greater, or the hæmorrhage is moderate in amount but repeated, the patient becomes pale and complains of giddiness, ringing in the ears and tendency to syncope. The temperature falls in proportion to the amount of the hæmorrhage. But this fall is only temporary, and the thermometer soon rises to a higher level than before the fall. Late hæmorrhages often indicate a fatal prognosis (30–35 per cent.), with rapid termination; in an hour in one of Trousseau's cases, and even in a few minutes (H. Vincent). Though some writers have regarded intestinal hæmorrhage in typhoid fever as a favourable symptom, actual facts and statistics prove, on the contrary, that it is a serious symptom, since 44·3 per cent. of the patients with this symptom succumb (Homolle).

Intestinal Perforation.—Intestinal perforation in typhoid fever may be single or multiple, and occur in mild, ambulatory forms as well as in severe attacks, and more rarely in the course of relapses. Their seat

of predilection is the ileum in its last 40–50 cm., especially in the neighbourhood of the ileo-cæcal valve, the appendix and large intestine as far as the rectum.

Perforation is more frequent in men than in women. It is rather rare in children. It occurs generally at the end of the second week, or in the course of the third, and even later. The efforts which patients make in raising themselves or using the bedpan are sometimes responsible for it.

Intestinal perforation is often heralded by premonitory signs, to which some writers attribute very great value and others very little.

Triboulet thinks that profuse diarrhœa accompanied by blood, even in slight traces, has a very great importance in enabling one to foretell intestinal perforation.

Meteorism should be interpreted with much reserve, for perforations have been seen to occur in collapsed intestines, and, on the other hand, very pronounced abdominal distension has been seen when there was no perforation (Cassaët and Duperié).

Intestinal perforation is revealed by peritonitis, which may run its course in one of two ways : acute or hyperacute peritonitis, or peritonitis with attenuated signs, and even latent peritonitis. In the majority of cases the onset is sudden and unexpected. The patient feels a very violent spontaneous pain which compels him to cry out, and may even make him lose consciousness. Without any obvious cause he feels a tearing or stabbing sensation in the lower part of the belly on the right hand side, which may radiate along the spermatic cord to the testicle and rectum and then become generalised. Sometimes the pain is less violent. It may be confined to a rather painful spot, over which slight hyperæsthesia is found on palpation.

Usually there is muscular contracture, which is at first localised to the lower part of the recti, especially the right rectus, and then rapidly extends all over the abdomen, which may assume a board-like hardness and show a scaphoid retraction. The patient usually has a severe attack of shivering; his face is drawn,

his voice lost, the nose pinched, his eyes sunken and surrounded by dark rings, and the extremities cold. The temperature shows a sudden drop, falls even below normal (Fig. 2), and remains so in the cases that are

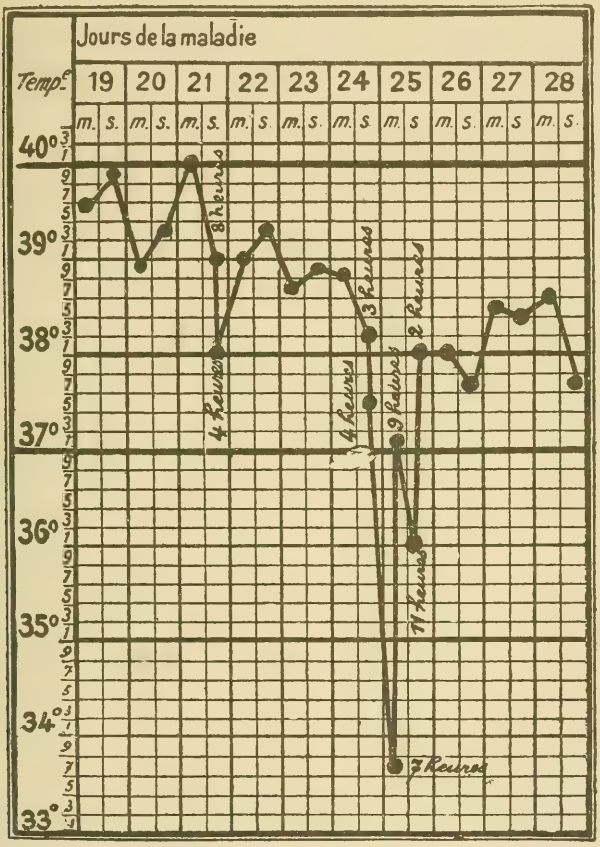


FIG. 2.—Hospital orderly. Typhoid fever, 25th day of disease. Signs of perforative peritonitis. Cyanosis, hypothermia. Temperature 92·6°. Recovery without operation.

rapidly fatal, or rises again a few hours later, but slowly and hesitatingly, in a very different way from the sudden ascent observed after intestinal hæmorrhage. This hypothermia is, unfortunately, not constant, being sometimes replaced by hyperthermia. Lastly, in some

cases the onset of peritonitis is not accompanied by any change of temperature.

The pulse may become frequent, small and feeble, or, on the contrary, become slow. The patient may have nausea and bilious vomiting, which is sometimes green and porraceous and appears early or late. There may be hiccough; micturition—when anuria is not present—may be painful. This vesical pain, which has been noted by Sieur, Picqué and Delbet, is a good sign if it occurs regularly.

The stools are much diminished, if not actually suppressed. This symptom, which has been noted by Sieur, although a late one, has all the more value, as at the period of perforation typhoid patients usually have numerous stools.

Inspiration of the costal type has been noted, as well as disappearance of the liver dulness.

According to Levaschoff, on auscultation a peculiar sound is heard due to the passage of gas into the abdominal cavity. Brown's signs have been rarely met with, and their investigation may be extremely dangerous for the patient. We will mention them, however, for the sake of completeness.

(*a*) The patient lying in the dorsal decubitus, one finds by palpation the point at which the maximum pain is felt. This point having been determined, if the patient be made to lie on his left flank, the painful spot becomes displaced at the same time as the intestinal mass, being shifted from $1\frac{1}{2}$ to 2 cm. in twenty to thirty minutes.

(*b*) If a stethoscope be suddenly applied to this point, fine crepitations are heard which indicate a localised peritonitis.

The sudden appearance of hyperleucocytosis in the blood is inconstant.

It is thus clear that there is no constant sign of intestinal perforation. We may, however, say with Faisans and Flandin that "we ought to think of perforation of the intestine when a pain occurs without any definite reason in a typhoid patient in the third

week, whether it be a stabbing pain or a dull pain, and whether situated at the umbilicus or in the right iliac fossa." The presence of certain other symptoms will confirm the diagnosis; but one should always remember that perforation may be insidious and develop almost without symptoms, and that "the advent of perforation may likewise be latent in consequence of the patient being delirious or unconscious; the prostration being accounted for by the severity of the fever, and the ordinary symptoms of peritonitis being absent" (Murchison).

Spleen

Enlargement of the spleen is almost constant. It begins in the middle of the first week and increases until the end of the second. It is an acute enlargement of infective origin, which may be accompanied by abscesses and hæmorrhages into the parenchyma, and, in exceptional cases, end in rupture of the organ. At first the spleen is firm and hard, but later it becomes soft and diffluent.

How are we to examine the spleen, and when can we say that it is increased in size? Normally it is situated behind the border of the false ribs, and is not accessible to palpation. Its outer and convex surface corresponds to the ninth, tenth and eleventh ribs. Its anterior border is thin and does not pass beyond a line drawn from the sterno-clavicular joint to the anterior extremity of the eleventh rib (sterno-costal line). It may be examined by percussion and palpation, which should always be carried out gently. The enlargement is more readily detected on percussion than on palpation. Percussion should be made gently with little taps and concentrically, starting from a sonorous region towards the zone presumed to be splenic, keeping the ear close to the percussing finger. In practice a spleen should be considered large which measures more than 5 cm. in the largest diameter of its dulness. It may reach nine, ten or twelve cm. and more in its largest axis.

Respiratory System

The *respiratory movements* are usually accelerated, apart from any pulmonary complications. They generally vary with the pulse and temperature.

The *nasal fossæ* are dry; *epistaxis*, varying in frequency and gravity, may occur at any period of the disease. Apart from cases in which it is only one of the manifestations of hæmorrhagic typhoid fever and those which are of exceptional gravity owing to its profuseness, epistaxis has no prognostic significance.

Typhoid fever very frequently causes lesions of the *larynx*, the two commonest of which are ulceration of the epiglottis and laryngo-typhoid. The patient usually has a little hoarseness or aphonia, with dysphagia, especially if the epiglottis is the seat of the ulceration, and the larynx is more or less tender on pressure.

In the course of ataxic or adynamic fevers with bedsores and multiple abscesses, more important lesions are found, consisting in necrosis of the larynx, or *laryngo-typhoid*. After a period of hoarseness the voice becomes weak, the respiration noisy and difficult, and deglutition painful. The patient has a hoarse and toneless cough, and cannot speak above a whisper. All these symptoms become rapidly more pronounced. The cough becomes croupy, the expectoration purulent, or blood-stained, and may contain fragments of necrosed cartilage, the breath is fœtid, the dysphagia increases, and pressure on the larynx is intolerably painful. Respiration becomes more and more difficult and is accompanied by a noisy, guttural rhonchus, which is sometimes "deadened, or rough and harsh like the sound of a bass string" (Bouillaud). Then occur an attack of suffocation with cyanosis, cold and clammy sweat, terrible anxiety, and cardiac failure. The attacks may be repeated, being provoked by the mere application of a tongue depressor or laryngoscopic mirror, or the absorption of a small quantity of fluid. In the intervals between the attacks the patient is in a

state of asphyxial collapse. In spite of a continuous dyspnœa, the suffocative attacks may be absent during the day, as an effort of the will is sufficient to maintain respiration, but at night during sleep, when the will is no longer active, the attacks begin.

The patient may die in an attack, or as the result of a sudden spasm of the glottis.

If he escapes death by asphyxia, he may have abscesses in the neck, necrosis of the cartilages, perilaryngeal phlegmons, etc.

Bronchitis is very frequent in typhoid fever. It generally appears at the end of the first week, and is revealed by sibilant *râles* mixed with a few mucous *râles* scattered here and there throughout the chest, but predominant at the bases. The cough and expectoration have no special characters. Sometimes the lesions of bronchitis are complicated by a slight degree of *pulmonary congestion*, with spasmodic cough and dyspnœa.

At the height of the disease, towards the third or fourth week, there may be *engorgement* and *splenization of the bases* without definite physical signs.

Pulmonary œdema may also be found, indicating typhoid nephritis. But the most frequent pulmonary complication is undoubtedly *broncho-pneumonia*, which may be present in 7 per cent. of the cases (Joffroy), and even 11 per cent (Nobécourt and E. Peyre).

Usually a late event, it develops insidiously, and should always be regarded as serious owing to its possible modes of termination, viz. extension of the process, phenomena of infection, suppuration and gangrene.

Pneumonia rarely occurs before the third or fourth week. In rare cases it may appear sooner and be taken for the initial disease. It has been described under the name of *pneumo-typhoid.*

At the height of the disease pneumonia singularly aggravates the condition of the typhoid patient. In convalescence it has not the same significance, as a rule.

Simple hæmorrhagic infarcts are fairly frequent; foci of pulmonary apoplexy are revealed only by hæmoptysis.

Lastly, *embolism of the pulmonary artery, multiple abscesses and pulmonary gangrene* have been recorded.

Pleura.—Pleural complications are far from rare in typhoid fever (2–4 per cent. according to E. Joltrain and G. Petitjean). They are even more frequent than is supposed, if they are looked for methodically. They may be observed at the onset of the disease, and they constitute that special form which has received the name of *pleuro-typhoid.*

But it is at the height of the disease, and especially in convalescence, that they usually appear.

Dry pleurisy in typhoid fever has no clinical history. *Serous pleurisy* chiefly occurs at the onset.

Cytological examination of the centrifugalised fluid shows an abundance of desquamated endothelial cells and neutrophil polymorphonuclears or eosinophils. In some cases the number of lymphocytes is very high and indicates a latent tuberculous infection, which has been made active by the typhoid bacillus (H. Vincent). Cultivation of the pleural fluid often shows the typhoid bacillus.

Hæmorrhagic pleurisy may be observed at the beginning of convalescence. It is due either to latent tuberculosis or to special virulence in the strain of the typhoid bacillus.

The last view seems to be confirmed by the fact that pure cultures of the typhoid bacillus injected into the pleura of guinea-pigs have produced an abundant hæmorrhagic effusion. Pleurisy may be hæmorrhagic from the first, and then purulent, and finally hæmorrhagic again. When it is localised it may be hæmorrhagic in one part with a B. coli of attenuated virulence, and purulent in another part with the typhoid bacillus (Macaigne and Théry).

The effusion is scanty as a rule and situated on the left. Its appearance and development are generally insidious, without pain in the side, dyspnœa, or rise

of temperature, and the diagnosis can be made by exploratory puncture only.

In addition to the presence of a large number of red cells, lymphocytes or neutrophil polymorphonuclears, which vary in number according to the case, cytological examination of the hæmorrhagic effusion shows a large proportion of large endothelial cells, isolated or in groups, which are to be found as long as the effusion lasts (Widal, Ravaut and Lemierre). Vincent found lymphocytosis in a hæmorrhagic pleurisy due to typhoid bacilli. In Rosenthal's case the initial lymphocytosis gave way to polymorphonucleosis. In Macaigne and Théry's case pus containing typhoid bacilli showed a very high polymorphonucleosis with the cells considerably damaged, without eosinophils and with only a few mononuclears.

These effusions, whether serous, sero-purulent or hæmorrhagic, do not present, as a rule, any gravity. Usually they are absorbed spontaneously, without puncture and without leaving any trace. It is not the same with purulent effusions, which may end in empyema, an interlobar pleural abscess, or a vomica.

Circulatory System

Pericarditis and *endocarditis* are fairly rare in typhoid fever. Ulcerative endocarditis with the typhoid bacillus both in cultures and in sections, has been recorded (H. Vincent).

Myocarditis is extremely common in the course of the third week. It is very important to look for it. It is observed especially in the graver and prolonged forms, or in the ataxo-adynamic forms with hyperpyrexia. Myocarditis is revealed at its onset by acceleration and enfeeblement of the heart-beat, by muffling of the heart sounds, especially of the first sound, fall in the blood-pressure and failure and irregularity of the pulse.

But these phenomena are soon replaced by the fœtal or tic-tac rhythm to which Huchard has given the name of embryocardia.

In this case the two silent intervals become of equal duration, and the two sounds have the same intensity and the same tone. There is at the same time tachycardia. The pulse becomes frequent, small and compressible, then unequal, irregular, intermittent, and sometimes alternating : *i. e.* at regular intervals a strong and normal pulsation succeeds one which is small and inadequate. At this stage the patient's urine is scanty and albuminous ; pulmonary congestion may be noted.

In a more advanced stage the cardiac impulse is replaced by an indefinite undulation (Hayem).

On auscultation there is considerable weakening of the first sound, which may disappear completely. The second sound is not modified in the majority of cases, but it may, however, be reduplicated and get weaker until it disappears (Hayem). One may hear a very soft murmur, meso-systolic or even systolic in time, situated at the apex and conducted to the base.

The patient complains of intense dyspnœa and has a distressing air hunger. His face is cyanosed and his eyes wander. His temples are covered by a cold, clammy sweat. The lower limbs become œdematous. The pulse becomes feeble and cannot be counted.

Soon an algid collapse develops, which may be transient, last a few hours and disappear, or be the cause of death, simply from cardiac insufficiency, without asystole.

On other occasions the patient dies suddenly on making a simple movement or slight effort, or in a syncopal attack, without a cry or complaint of any kind. A syncopal attack is not necessarily fatal, but in cases which survive it aggravates the prognosis ; the patient will often develop chronic myocarditis, which sooner or later will lead to asystole.

It is necessary, therefore, to make a systematic examination daily for myocarditis. Knowledge of this frequent complication is of the utmost importance to the practitioner.

Veins—Typhoid Phlebitis. Thrombo-Phlebitis. Phlegmasia alba dolens

The type of typhoid phlebitis is the phlebitis of the veins of the lower limb, or *phlegmasia alba dolens*. Due, as a rule, not to the typhoid bacillus, but to the staphylococcus, the thrombosis affects principally the femoral vein, less frequently the saphenous and popliteal. It is more often unilateral than bilateral, and is almost always situated on the left. Trousseau thought it was rare, Murchison found it in 1 per cent., Hutinel in 6 per cent., Vincent in 8·23 per cent. among 340 cases of typhoid fever, and Da Costa in 12 per cent. Conner says, "If we can succeed in recognising the attenuated forms, it will probably be found in 10–15 per cent."

Phlebitis is a complication of convalescence, almost always occurring in the week or fortnight following the disappearance of the fever.

The onset is sometimes gradual, sometimes sudden with sharp pain and pronounced rise of temperature. The signs are those typical of phlebitis, with this difference, that the hard œdema is not white but is accompanied by a slight redness. Recovery takes place as a rule, but any of the complications may develop which have been noted as the sequel of any venous thrombosis, such as varicose veins, œdema, gangrene, pulmonary, cardiac or renal embolism, and sudden death.

Conner thinks that the typical symptoms do not appear till late, when the venous obliteration is an accomplished fact. He also regards the pleuro-pulmonary complications of typhoid fever as embolic in origin. The emboli are derived from friable thrombi, recently formed in veins which have not yet been obliterated, which would explain why their manifestations appear before the typical signs of phlebitis. The typical symptoms of these embolisms are—

1. An almost constant pain in the thorax, almost

invariably at the onset, appearing suddenly, and situated in the lower part of one of the axillæ.

2. Constant cough, with occasionally blood-stained expectoration (45 per cent.).

3. Oppression, dyspnœa, shivering and signs of pleurisy, with or without effusion, may be noted.

4. Finally, Conner insists on the value of a sign which he has found in all cases of confirmed or latent phlebitis, viz. *pain in the toes*, resulting from "an irritation of the plantar nerves due to a periphlebitic inflammation in the neighbourhood of the thrombosed veins in the region of the heel."

Perhaps a more simple explanation would be peripheral neuritis.

Arteries. Typhoid Arteritis.—Typhoid fever occupies the first rank among the infections which are the cause of arteritis. Like phlebitis, this arteritis is usually found in the lower limbs, but, unlike phlebitis, chiefly on the right side. The posterior tibial is the artery most frequently affected, and then the femoral, popliteal, anterior tibial and dorsalis pedis. Then come the arteries of the upper limbs, the iliacs, external carotid, Sylvian, etc. Arteritis of the limbs hardly ever occurs before the end of the third week, from the thirteenth to forty-first day (Rendu), or even up to the fifty-eighth (Barié), whereas arteritis of the visceral arterioles, which is much more frequent, is generally observed during the height of the disease.

The typical arteritis of typhoid fever—viz. that in the lower limb—begins with a pain which is more or less acute and sudden, but is always situated in the course of the arteries. Sometimes it is localised in the calf, the popliteal space, or Scarpa's triangle, but it may occupy the whole limb. It is greatly aggravated by walking, compression, standing, or the least movement.

The amplitude of the pulsation in the affected arteries is very much diminished, sometimes even the pulsation is entirely suppressed. The lower limb affected is first of all swollen, but without œdema or redness. Then it becomes mottled with violet patches, areas of

cyanosis, and even purpuric spots. The patient suffers from formication and other uneasy sensations in the leg, which grows cold.

The artery appears in the form of a hard and painful cord. Finally, dry gangrene, which terminates the process, involves elimination of the mortified tissues and death. In rare cases venous thrombosis may be observed at the same time as the obliterative arteritis (Patry).

Cases are on record of *parietal arteritis*, i.e. partial arterial obstruction, or narrowing of greater or less extent of the lumen of the vessel, in which the previous symptoms are attenuated and the lesions curable. When the arteritis affects other vessels than those of the lower limb, the gravity of the terminal gangrene is due to the functional importance of the organ supplied by the affected artery.

Blood.—During the febrile period a reduction of 70–80 per cent. in the amount of *hæmoglobin* may occur, and in grave cases it may fall even below 70 per cent. The number of red blood cells is slightly diminished during the first two weeks ; a slight increase in their number, however, has been recorded. On the average the red cells number from 4,000,000 to 5,000,000 during the febrile period. At the time of defervescence there is a sudden diminution of the red cells. In severe forms this may be considerable : 804,000 red cells per cubic millimetre (Henry).

The *changes in the corpuscles* are of the ordinary kind : microcytes, megalocytes and polychromasia. After hæmorrhage some nucleated red cells have been seen.

The *colour index* is almost normal. Hénocque and Baudouin have seen the *activity of reduction for oxy-hæmoglobin* fall spectroscopically to 0·20 during the height of the disease, rising to 0·50 in convalescence and to 0·70–0·80 on recovery. Pignatti and Morano have seen an *increase in the mean resistance* of the red cells at the height of the disease, with a more or less sudden return to normal, and sometimes even diminution, in convalescence.

The *absorptive power* of the blood for oxygen is diminished (192–196 cc. of oxygen for 1000 grm. of blood instead of 240 cc.). The *leucocytes* have formed the object of numerous researches. It is well known that in normal conditions very slight causes are sufficient to cause variations, not only in the total number of leucocytes, but also in the differential count. It is therefore not surprising that the results published do not admit of comparison owing to the extreme variety of the cases, complications and incidents of all kinds, as well as the treatment, which may modify the result of the examinations.

Apart from differences of detail, it may be affirmed that typhoid fever does not increase the number of leucocytes. It may even cause a *leucopenia*, which disappears rapidly or slowly, once and for all, or on several occasions, either at the time of convalescence or a little before.

In the course of the first week the differential count shows an excess of polymorphonuclears, in the second and third weeks there are lymphocytosis and mononucleosis, with disappearance of the eosinophils. At the same time there appears in half the cases an iodophil reaction in the leucocytes, but we believe that its appearance coincides with the onset of complications, especially of an inflammatory nature.

From the prognostic standpoint the examination of the blood may furnish the following valuable information—

1. The reappearance of the eosinophils indicates the onset of convalescence within two or three days.

2. A rapid increase in the number of leucocytes may indicate a complication. This complication is of an inflammatory nature when the increase in the number of the leucocytes is accompanied by polymorphonucleosis, with an iodophil reaction.

3. A rapid and very pronounced decrease in the number of leucocytes indicates an aggravation of the disease, especially if it is accompanied by a diminution in the number of lymphocytes.

The blood platelets diminish in number until only 50 per 100,000 are found at the time of defervescence. Then they slowly increase, following an ascending curve, which attains its maximum twelve days after the end of defervescence (Hayem).

The *alkalinity* of the blood rises at the onset of typhoid fever, and then undergoes a progressive diminution.

The *coagulation time* does not show any remarkable modifications; it is, perhaps, a little delayed.

The *clot* is soft, forms slowly, sometimes even incompletely. The *amoumt of fibrin* varies from 1 gm. to 3·7 gm. per 1000, and sinks in proportion to the gravity of the disease.

Some importance has been attributed to the investigation of the fibrin network, between the slide and coverslip, according to Hayem's method. The absence of the fibrin network, or the slenderness of the fibrin threads, is not peculiar to typhoid fever; they are met with in a number of other febrile conditions, and especially in the eruptive fevers and acute miliary tuberculosis.

The *serum* which exudes from the clot varies considerably: it is abundant, clear and lemon-yellow when the clot is well formed, and its retraction is normal; it is somewhat scanty, and of a reddish colour when the clot is soft, retracts slowly and more or less completely. It may be lactescent.

The important characteristic of the blood serum in typhoid is the property which it possesses of agglutinating the specific bacillus from the moment of invasion. It is upon this idea, which is due to Widal, that the "serum diagnosis" of typhoid fever is founded.

Reserving for our special chapter on the laboratory diagnosis of typhoid fever a description of the technique of the serum test and the conclusions to be drawn therefrom, we will confine ourselves here to a consideration of the clinical significance of agglutination. Let us state first of all in what it consists. The phenomenon may be seen both microscopically and macroscopically.

If to 100 drops of a young culture (24 hours) of the typhoid bacillus be added a drop of typhoid serum, in a few minutes the microscope will show that the bacilli have lost their motility and are grouped in more or less considerable masses, between which may be seen a few isolated, but motionless, bacilli. If the mixture has been made in a small tube and put in the incubator, the fluid, which was turbid at first, becomes clear, and whitish flakes become deposited at the bottom of the tube. This agglutination reaction is specific; that is to say, peculiar to the typhoid bacillus.

Nevertheless, the serum of patients suffering from paratyphoid A can agglutinate indifferently the typhoid bacillus and the paratyphoid B bacillus (Sacquépée).

The serum of patients suffering from paratyphoid fever contains, in fact, fairly often coagglutinins and *cosensibilisatrices* (Rieux and Sacquépée).

This is the reason why exact information can be furnished by a blood-culture only. In the absence of a blood-culture, in non-vaccinated subjects the agglutination test should be used for the diagnosis of typhoid fever.

Normally the human blood serum does not contain an agglutinating power higher than 1 : 10 or 1 : 20. This power appears after anti-typhoid vaccination (1 : 50 to 1 : 10,000).

In pathological conditions it often appears in the course of the proteiform manifestations produced by the typhoid bacillus : such as typhoid fever, typhoid icterus, meningo-typhoid, etc. Generally speaking, the reaction in typhoid fever usually appears towards the seventh day. Widal has sometimes observed it on the third day. In the course of the disease the curve of agglutinating power is infinitely variable and unforeseen (Rouget). It persists for a varying period, such as a few months, or, more rarely, three years, six years, or as much as twenty-six years after the disease, and sometimes with remarkable intensity (1 : 8000 in a patient described by Widal and Sicard, who had recovered from typhoid eight years previously). Its appearance may be delayed till the second or third

week; it may appear only in convalescence or in the course of a relapse (Thoinot and Cavasse). Lastly, it may be absent altogether.

The serum may retain its agglutinating properties for three or four months after desiccation. This fact is important to know in view of a retrospective diagnosis or of a medico-legal report. The agglutinating reaction may pass from the mother to the fœtus (Widal and Sicard), but this passage is inconstant and incomplete.

Experimentally, the *sensibilisatrice* may be found in a young rabbit born of an infected mother (Vincent and Marbais).

The great variability in the appearance of the agglutinating reaction, in spite of its specific value, has induced the clinician to seek in the blood for the actual cause of the reaction which indicates the infection. This investigation is carried out by a *blood-culture*, with which we shall deal later.

It has been found that the blood plasma, fluid from blisters, nurse's milk, tears, aqueous humour, bile, fluid from œdema and inflammatory serum may possess specific agglutinating properties of varying intensity in the course of a typhoid infection.

The *toxicity* of blood serum may be considerable in the course of the second week of typhoid fever, whereas it is normal in the first and third weeks.

The *hæmolytic power* of the blood is increased in typhoid fever. The *attenuation of certain blood ferments* is a very grave symptom, and as a rule the herald of a rapid termination (Achard and Clerc).

The Pulse and Temperature

The study of the changes in the pulse and the temperature curve are not only valuable elements in diagnosis, but when the diagnosis is established it is by them chiefly that the medical man can judge of the course of the disease, appreciate the patient's resistance, establish an immediate or remote prognosis and decide to intervene or abstain from treatment. The

pulse and temperature should be so frequently compared with each other that, contrary to the plan adopted in this work, it appeared to us to be of real practical interest to study them here side by side. It may also be well to recall the normal and physiological characters of the pulse and temperature, so as to illustrate their variations in the course of typhoid fever.

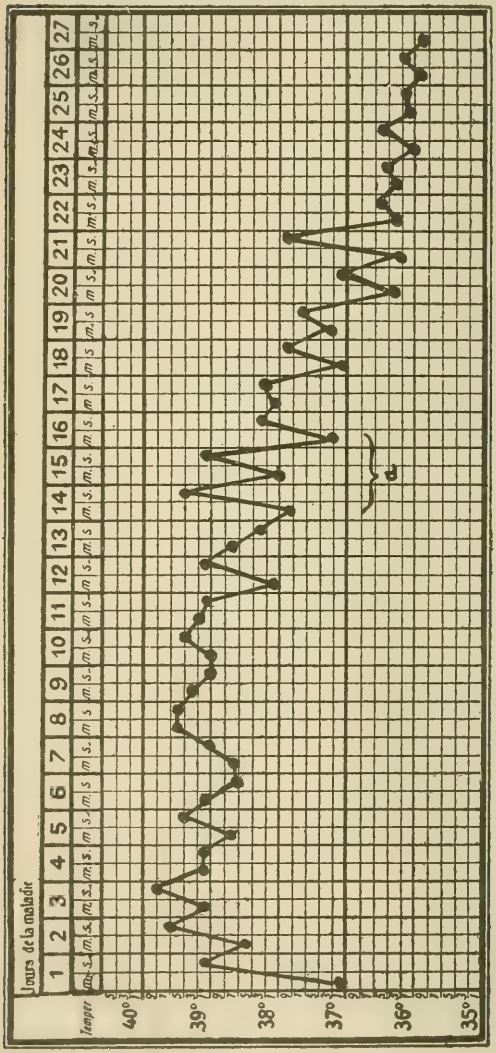


FIG. 3.—Typhoid fever. Temperature taken from the first day. Sudden onset. *a*. amphibolic stage.

Pulse. — Normally, the rate of the pulse is, on the average, 120 per minute in an infant a year old, 100 in a child of three years, 80 in a child of 8–10 years, and 70 in an adult.

It becomes more rapid in the first weeks of typhoid fever; it remains rapid at the height of the disease, and loses its frequency in defervescence.

The acceleration, which is more pronounced in

women and children than in the adult, varies considerably.

" Out of 100 cases, I ascertained that it exceeded the normal standard, at some time of the fever, in all but 1; in 97 cases it exceeded 90; in 85 cases it exceeded 100; in 70 cases it exceeded 110; in 32 cases it exceeded 120; in 25 cases it exceeded 130; in 10 cases it was above 140; and in 2, above 150 " (Murchison).

The frequency of the pulse undergoes great variations from one day to another, and even at different hours of the same day. In the evening there may be 10–30 beats more than in the morning.

The pulse is accelerated by a pulmonary complication or an intestinal hæmorrhage.

As a general rule, the severest cases are those in which the pulse is most rapid, and usually it is a bad prognosis when the pulse in the adult keeps above 120–130 (Fig. 1). In some cases the pulse may be very slow (as low as 37 beats per minute), or never vary from the normal.

Irregularities of the pulse (arrhythmia, intermittence) are not rare.

Characters of the arterial wave. Dicrotism.—At the onset of the disease, during the first eight or ten days, the pulse is strong, full and of good tension, but soon it becomes soft and compressible. At a more advanced period it may be small, feeble, undulating, irregular, intermittent or imperceptible.

One of the most remarkable characters of the typhoid pulse at the height of the disease is *dicrotism*. It is well known that on sphygmographic tracings the cardiac systole corresponds not only to the line of ascent but also to the line of descent. The arterial pressure, in fact, increases until the moment when the heart suspends its systolic effort, and the pressure falls only at the moment when the sigmoid valves of the aorta close. The impact of the column of blood on the valves is indicated on the descending line of the tracing by an undulation which is called " the rebound of the pulse," or " dicrotism." Dicrotism, therefore, is a normal element of the pulse, too weak to be felt by the finger, but

strong enough to be registered on the sphygmographic tracing. In typhoid fever this dicrotism becomes exaggerated until it becomes perceptible to the finger. It increases in proportion to the weakness of the arterial pressure and the rapidity of the heart-beat. Cold baths may cause it to disappear; its return may indicate a threatening hæmorrhage (Paviot).

The arterial pressure is very low in the typhoid patient (Potain), but this fall is only of secondary importance, the changes in the arterial pressure being related to the frequency of the pulse (Azelais).

Temperature.—It is well known that in the healthy man the rectal temperature varies at different hours of the day. On waking up at six o'clock in the morning it is, on the average, 98·4° F. It rises progressively to a maximum which varies from 99·0° to 99·5° at about seven p.m., and then sinks to a minimum of about 98·0° F. towards three or four a.m., to rise later. We may say here that, normally, the excursions of the temperature are, on the average, a degree and a half.

The same daily variations occur in typhoid fever, but the excursions are more marked.

In this disease the morning temperature oscillates generally between 103·2° and 104° F., and the evening temperature between 104° and 105·2° F. The fluctuation is from 0·8° to 2° F. But these oscillations may be greater, and at the height of the disease be as much as 3·6° F. Lastly, in some cases the temperature tends to return to the normal level; it rises again in the evening, and the great oscillations which result therefrom constitute the *amphibolic* stage of Jaccoud.

Charts may also be seen in which the maximum temperatures occur in the morning and the minimum in the evening. These *inverse types* never appear throughout the extent of the febrile cycle.

Their significance is not known apart from the cases in which the patient is suffering simultaneously from malaria or tuberculosis, or has been treated by antipyretic drugs.

But the clinical importance of the cyclical course of

temperature is even greater than its daily variations. Typhoid fever may be classed among those diseases in which the temperature curve usually pursues the same, or almost the same, course. There is, however, nothing absolute about it, for a slight complication is enough to modify the temperature curve and disguise it effectually.

Ordinary Course of the Temperature in Normal Typhoid Fever.—In the *incubation period*, in quite exceptional cases, a slight pre-febrile temperature may be noted, usually in the evening, sometimes also in the morning, reaching 99·6° or 100,° but never exceeding 100·4° F. (Vaucher and Dufour, Roch).

Starting with the truly clinical period of typhoid fever, the temperature curve may be schematically compared, according to Jaccoud, to the three upper sides of a trapezium. The oblique ascending line corresponds to the period of onset, or *ascending oscillations;* the horizontal line corresponds to the height of the disease, or *stationary oscillations;* and the oblique descending line indicates the period of decline, or *descending oscillations.*

At the period of onset (Fig. 4) the temperature rises progressively and slowly, exceeding each evening, by a degree or more, the corresponding temperature of the evening before, with a morning remission which also keeps above the record of the previous morning by one or more degrees.

These ascending oscillations are rarely seen in the army, as the patients come to the doctor too late.

In about four days of this staircase-like ascent the temperature is about 103° F. It keeps at this level during the two weeks which constitute the ordinary duration of the height of the disease. During this period the morning remission varies from 1° to 1·8° F. at most. The temperature curve may then be compared to the serrations of a saw, the base of each serration being 102·2° and the point about 103·0.°

However, at the onset of this period of stationary oscillations, and especially about the sixth or seventh

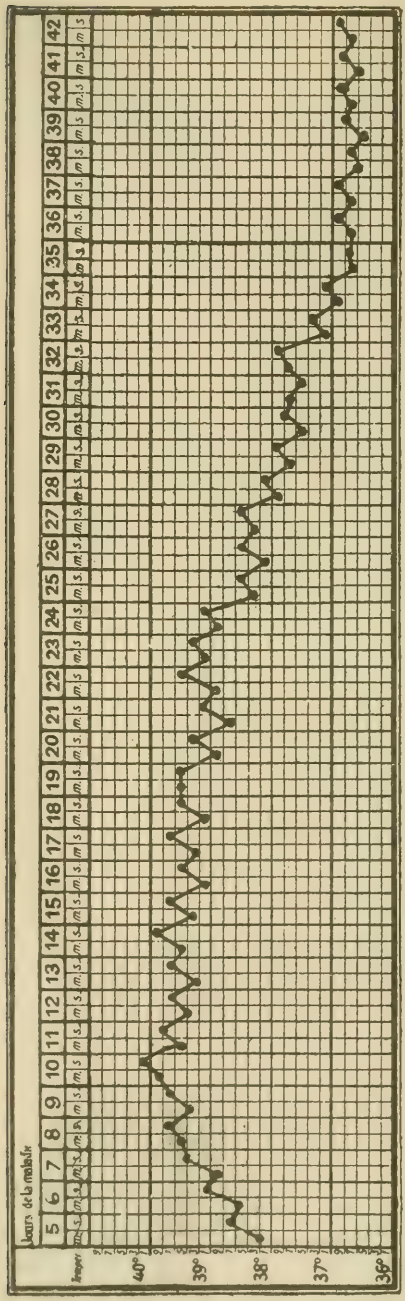


FIG. 4.—M. L. aged 22 years. Late and sudden death from myocarditis on 56th day.

day, a fall of temperature nearly to normal is very often seen, constituting a sort of sudden and temporary remission, varying from 1·8° to 4·4°, and only lasting from ten to twelve hours on the average. It is probably a sort of *thermic crisis* which indicates a defensive state of the organism, for at this moment the existence of antibodies in the blood may be first noticed.

During the height of the disease the temperature shows a certain stability. The fastigium of typhoid fever has been called by the name of *plateau*. During this period the evening rise ranges between 104·2° and 104·8°, the morning temperatures being, on the average, 0·8° to 2·6° lower. The height of the disease, in the majority of cases, presents a single plateau, but this plateau may be divided into two, each lasting a week, the second being a little above or below

the first. In severe cases the temperature curve is irregular, capricious and steep, with temporary rises and falls of grave prognosis.

It is especially in warm countries that such cases are seen. Sometimes the fastigium is prolonged to the third or fourth week.

It is at this period that the *amphibolic stage* of Jaccoud must be placed (Fig. 3). It is formed by oscillations of great amplitude succeeding one another without any order for three or four days, and giving the curve a hesitating and uncertain character, and followed by frankly febrile temperature and actual hypothermia. If the termination is to be fatal, the temperature rises to 107·6° and even higher (109·4°), or, more rarely, it falls considerably until death, which takes place from collapse.

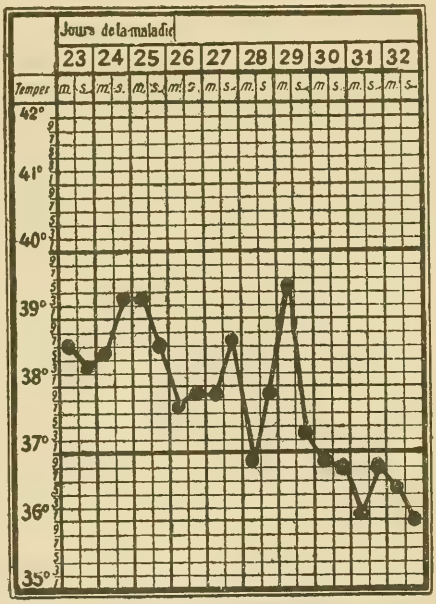


Fig. 5.—Meningeal symptoms (delirium, coma, strabismus, etc.) towards the end of typhoid fever on 27th day. Sudden defervescence.

In favourable cases, whatever may have been the duration and form of the fastigium, *defervescence* occurs in one of two manners: slowly and gradually by lysis, or suddenly. Sometimes, though rarely, a crisis is seen, characterised by very unusual nervous symptoms resembling those of meningitis (Fig. 5). In defervescence by lysis the curve is exactly the reverse of that of the ascending oscillations. The descent is made by steps constituting a sort of "exit staircase" for typhoid fever. In cases of sudden

defervescence this stage of descending oscillations may be entirely suppressed (Fig. 5). Very frequently, after an apyrexial period of a few days, a slight hypothermia (98·0°–98·2°) may be found, which is more pronounced in the old and debilitated, and after long and severe fevers, and may sink to 96·8° and even 95·8.° In a few days the temperature becomes normal again.

Such is the typical chart of the temperature in normal typhoid fever, which is fairly often realised. It may undergo numerous variations. The onset is not always progressive: it may be "brutal," the disease may "explode" (Guéneau de Mussy), and the temperature may in this case jump from 98·6° to 104°, imitating the onset of pneumonia.

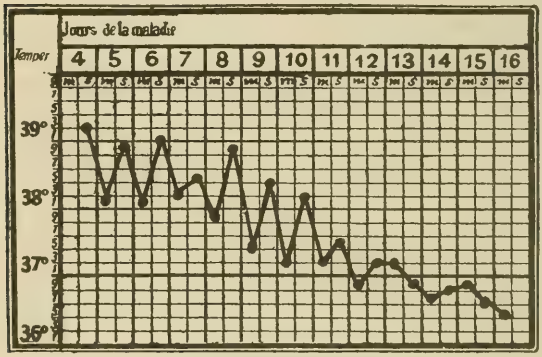


FIG. 6.—Hospital orderly. Mild typhoid fever. Defervescence by lysis.

It is well known that paratyphoid fevers frequently have a sudden onset.

In certain grave forms (ataxic and ataxo-adynamic) the temperature curve is extremely irregular. The temperature of the plateau is 104° and above.

Contrasting with these hypothermic forms are others in which the temperature is but little raised, and in which the plateau oscillates between 100·4° and 101·2°. There are also absolutely apyretic forms of typhoid fever in which the temperature is 98·6° or 99·4° throughout the whole course of the disease (H. Vincent). Lastly, Potain has recorded a case of hypothermic typhoid in which the temperature fell from 98·6° to 97·2°, where it remained until convalescence, when it rose again to 98·6°.

Certain events contribute to modify profoundly the

regularity of the temperature curve, some causing a rise and others a fall.

Complications which raise the temperature are numerous. At the onset these are the secondary infections of the pharynx, and a superadded disease (influenza, diphtheria, erysipelas, etc.).

At the height of the disease they are the pulmonary complications (bronchitis, broncho-pneumonia) bedsores, suppuration of the skin, otitis, parotitis, abscesses, phlebitis, peritonitis by propagation, etc. In convalescence they are errors in diet, fatigue, lesions of the bones or periosteum, constipation, return of the menstrual period in women (the last may give rise to false symptoms of peritonitis), etc.

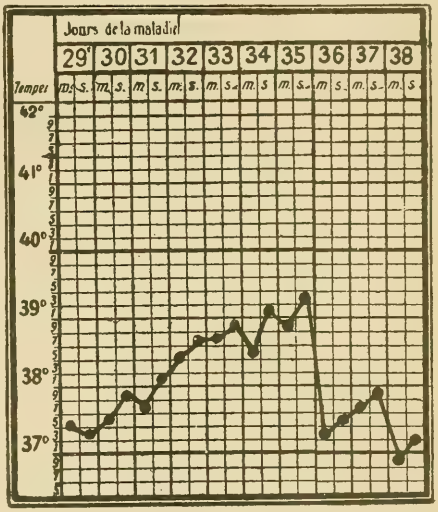


FIG. 7.—Man, aged 59. Typhoid fever in course of recovery. Formation of a renal abscess (staphylococci and typhoid bacilli). Spontaneous opening of the abscess on 36th day.

Among the complications which may cause a fall of temperature, the most important are hæmorrhages (intestinal hæmorrhage, profuse or repeated epistaxis, delivery or abortion), perforation, myocarditis, profuse diarrhœa, extensive bedsores, etc.

Relations between the Temperature and the Pulse.—As a general rule, in febrile conditions if the temperature rises a degree (1·8° F.), the pulse increases by about fifteen beats.

In typhoid fever a high temperature has corresponding to it a pulse which relatively is but little accelerated. A change in this formula in the sense of acceleration of the pulse is a grave sign. Thus a temperature of 105·8° is not a bad sign if the pulse is not accelerated. On the

other hand, the prognosis is gloomy if the pulse and temperature rise simultaneously.

A low temperature and a rapid pulse should be regarded as a grave case. If the temperature falls and the pulse becomes rapid, one should think of the possibility of intestinal perforation or hæmorrhage.

Lastly, if in the course of a regular defervescence by lysis an increase in the number of pulse-beats is found, the possibility of a cardiac complication should be considered.

Nervous System

Typhoid fever, like all infectious diseases, is liable to affect the nervous system.

The central anatomical lesions which cause these symptoms, and are due to the toxins (exo- and endotoxins) secreted by the typhoid bacillus, are still entirely unknown to us. Direct injection of the typhoid toxin into the brain of a dog causes complete necrosis of the nervous tissue. But that is a case of a gross and experimental lesion.

The nervous symptoms appear at a variable period of typhoid fever. They disappear, become attenuated or persist after recovery. Sometimes the nervous manifestations dominate the clinical picture, thus justifying the creation of special forms such as the ataxic, ataxo-adynamic, delirious, comatose, etc.

In predisposed subjects the infection provokes the appearance, aggravation or return of latent nervous defects, which have been attenuated or apparently cured. Lastly, it acts as a provocative agent in certain neuropathies.

All these manifestations we must now consider in detail.

Nervous Symptoms.—These may be classified as follows—

1. Symptoms of an ordinary kind if considered individually, but as the result of their special grouping

in typhoid fever, forming a peculiar syndrome which has been given the name of "*typhoid state.*"

2. Psychical disturbances.
3. Sensory troubles.
4. Motor troubles.
5. Meningeal syndromes (meningitis and meningism or meningeal states).
6. Troubles of the organs of special sense.

1. **Typhoid State.**—The nervous symptoms of the typhoid state are *prostration*, *stupor*, *insomnia*, *somnolence*, *tremors or muscular twitchings*, and *carphology*.

Prostration, Stupor, Insomnia, Somnolence.—Prostration exists in every case, but in variable degrees. Sometimes the patient really seems like an inert body (Louis), unable to move in bed or attend to his needs. Other patients, on the contrary, can sit up in bed, get up to go to the closet, and even attend hospital for advice.

Prostration is sometimes a symptom of the onset, especially in warm countries, or in soldiers in war time. As a rule it appears late in the course of the second week, becoming pronounced towards the end of that week or towards the middle of the third week.

Sphincter troubles are closely associated with prostration. The stools and urine escape involuntarily; retention of urine, necessitating employment of the catheter, is much rarer. During the first eight or ten days of the disease the patient cannot sleep, or his sleep is much disturbed by dreams and nightmares.

Somnolence immediately follows insomnia, at the beginning of the second week, but it may be observed from the onset. It may be slight, moderate or deep. Sometimes the patient wanders at night, while in the daytime he remains dull and drowsy, with his eyes half closed and a vacant look; he remains in a somnolent state, with intervals of delirium. The graver the case, the earlier, the more intense and the more prolonged is the somnolence (Louis).

The typhoid patient may often have what has been

called the "typhoid facies;" the face is pale, with a circumscribed flush on one or both cheeks, the expression is one of prostration and stupor, the pupils are dilated, and the eyes sunken. He is incapable of any rational act, and indifferent to persons and things, but in a varying degree. He has difficulty in putting out his tongue, but once protruded he leaves it in its new position.

Tremors and muscular twitchings.—Murchison noted tremor of the hands, tongue and lips in twenty-seven out of a hundred cases. He also found subsultus, contractions of the mouth and hiccough in some cases. Children may have choreic movements.

In the course of the present war R. Mercier and R. Meunier found in 68 per cent. of the cases (175 soldiers) continuous tremors, with periodic exacerbations characterised by rapid oscillations (8 per second) of moderate amplitude, with a maximum amplitude in the acute stage. These tremors were independent of the will, and purely reflex, and were present at all periods of the disease. They were most pronounced in soldiers who had undergone much fatigue.

Carphology.—It is not uncommon to find automatic movements in typhoid fever. Children constantly put their hands to their nose and bite their lips till they bleed. Some patients push off their bedclothes and try to get up, or continually put their hands on their genitals. But the most frequent of these automatic movements is that known by the name of *Carphology*. The patient "moves his hands to and fro above his bed and seems to be groping for small objects hanging in the air, or to be constantly looking for them in his bedclothes, from which he pulls out the nap." This continues, without interruption, for hours. Cold-bath treatment has much reduced the frequency and gravity of the stupor and other nervous phenomena accompanying typhoid fever.

2. **Psychical Disturbances.**—*Delirium.*—Delirium is frequent in typhoid fever, especially in subjects who are nervous, depressed, overworked, alcoholic, or

in a state of exhaustion. At the onset the patient's sleep is broken and he suffers from nightmare. In the daytime he gives himself up to monotonous reverie. At the height of the disease the delirium is at first quiet, and presents the oneiric character peculiar to infective and toxic delirium (Régis). It is often nocturnal. The patient mutters incoherent words in a sort of dream, and in the morning ends by going to sleep.

The delirium afterwards becomes diurnal, and then both diurnal and nocturnal; the prognosis is now more serious, even if the delirium is a peaceful one. But in some cases it becomes violent. It is accompanied by cries and disorderly movements, and above all it becomes an active delirium; the patient gets out of bed, tries to escape and has to be restrained. According to Régis, these are examples of acute psychosis with terrifying hallucinations—ideas of persecution, religious mania and megalomaniac ideas.

Subjects without any predisposition show an active delirium with a melancholic state, or a profound stupor with considerable mental excitement. The psychosis of the predisposed is a real acute delirium of extreme gravity, with muscular agitation, inco-ordination, tonic or clonic convulsive attacks, and albuminuria, which may end in collapse. In short, it is some form of mental confusion, such as hallucinatory delirium, stupor or acute delirium.

Lastly, in the course of every war varieties of delirium have been observed which Devaux and Logre have called by the name of "war delirium." Their theme is essentially a military one, such as dreams and visions of fighting, conversations and discussions about strategy, grim and fantastical stories of massacres or deaths on the field of honour followed by resurrections, scenes of the trenches or the battlefield, cries, restlessness, the patient asking for his gun and wanting to fight; ideas of military glory, melancholy ideas of guilt, of sentence by a court-martial and execution; struggles with imaginary enemies,

Uhlans, spiked helmets, etc. These symptoms of mental confusion show how deeply the patients' minds have been impressed by the war, which, with its picturesque and dramatic features, forms almost the only object of their professional delirium.

In convalescence some patients continue to suffer from the same psychical disturbances as they had during the height of the disease. When they occur at this time, and are not due to the administration of caffeine, these disturbances are due to inanition, and disappear as soon as the ordinary diet is resumed.

Typhoid fever, however, may be followed by the appearance or return of transitory or permanent mental disorders, such as mania, or chronic insanity assuming the hypochondriac, religious, melancholic, erotic, or even ambitious form. Mental degeneration, various forms of insanity, and general paralysis also occur after typhoid fever. As a rule, the intellectual and affective faculties are weakened, and memory and attention are considerably impaired.

3. **Sensory Troubles.**—The disturbance of general sensibility shows no peculiar features; sometimes one finds cutaneous anæsthesia, and sometimes hyperæsthesia due to neuritis, especially in the lower limbs.

At the period of onset the patient has pains all over the body, down the spine, in the limbs, especially the legs, in the epigastrium, the nape of the neck, and the joints. At the height of the disease the pain disappears or improves.

There is, however, one symptom whose frequency, early appearance and duration entitles it to a special description: viz. headache.

Headache is one of the first and most constant symptoms. It is usually very intense during the first week, and the patient attributes his insomnia to this cause. It is usually frontal, but is sometimes occipital and may be generalised and accompanied by hyperæsthesia of the scalp. It is generally a dull and wearing pain, without any sharp or stabbing characters. In most cases the patient is unable to work or think;

noise, light and smell affect him most disagreeably, he feels giddy when he changes his position or sits up in bed.

In moderate cases the headache lasts throughout the disease, in severer cases it disappears as the patient sinks into a condition of stupor. Lastly, in some of the so-called ambulatory cases, headache is often the only symptom.

Giddiness disappears with the headache, but returns, with or without it, at the beginning of convalescence.

4. **Motor Troubles.**—Whereas the sensory disturbances at the period of onset are specially localised in the lower limbs and the spine, the motor disorders are localised in the upper limbs, trunk and neck. The patient has *spasms* and *convulsive movements*, such as trismus, strabismus, hiccough, etc. *Generalised convulsions* are rarer than in typhus and less frequently of a uræmic nature. Some patients have *epileptiform attacks*, in which they foam at the mouth and bite the tongue, the attacks being preceded by acute delirium and followed by profound prostration.

Aphasia has been observed in the adult, and more frequently in the child, during the course of the disease or in convalescence, but this symptom is of short duration and may last only twenty-four hours.

Acute polioencephalitis has been noted in subjects under two years of age. Its pathogeny is still obscure. The onset is sudden and characterised by convulsions, vomiting and fever. Then it is noticed that one half of the body has become paralysed. The paralysis is most marked in the arm; the face is rarely affected. The parts affected show maldevelopment, so that shortening of the arm, amounting to five or six cm., may result from the infection.

The *reflexes* are exaggerated; *contractures* are exceptional.

Sometimes the patient suffers from *partial epilepsy*, or, more frequently, *hemi-athetosis* with mental disturbance.

The typhoid toxin is liable to cause extensive lesions

in the cord. Typhoid myelitis may assume the type of *acute ascending paralysis*, or *Landry's disease.* In some cases the initial symptoms are attributed to influenza or gastric derangement. In others the myelitis is characterised by pains in the trunk and limbs, anorexia, shivering and, above all, by fever.

At the height of the disease enlargement of the spleen is a guide to diagnosis. Death is the ordinary termination of the disease.

Typhoid fever may be followed by all the known types of *paralysis*, as is the rule after all infections. But post-typhoid paralyses are characterised by the motor troubles being usually incomplete, and being accompanied by various sensory disturbances.

5. **Meningeal Syndromes.**—*Meningitis, Meningism or "Meningeal States."*—We will not deal here with the *primary meningitis*, which is one of the forms of typhoid septicæmia due to localisation of the specific bacillus in the meninges. Nothing differentiates it clinically from acute cerebro-spinal meningitis; diagnosis can be made only by examination of the cerebro-spinal fluid.

The most frequent meningeal symptoms in typhoid fever are those observed at the height of the disease, from the sixth to the twentieth day, and more rarely in convalescence or in the course of a relapse.

The onset may be sudden and violent, but is more often insidious. Sometimes all the symptoms of the *meningeal syndrome* are present, viz. *headache, photophobia, pain in the spine, vomiting, contractures, and gun-hammer position.*

In children the picture is frequently completed by convulsive attacks which may give rise to a special eclamptic form. But as a rule the picture is incomplete, only headache and rigidity being present, together with Kernig's sign, which is constantly found.

As isolated symptoms, bradycardia, tachycardia, hiccough, sudden amaurosis and ocular palsies have been noted. Sometimes there are severe forms of true typhoid meningitis (meningo-typhoid), with a

turbid or purulent cerebro-spinal fluid, containing the typhoid bacillus. Sometimes the fluid is clear. The disease should then be regarded as an example of the meningism of Dupré, and this meningeal state disappears spontaneously or after lumbar puncture. Or, again, when there is nothing to suggest the onset of typhoid fever, but there are merely vague symptoms of a general infection, or even no prodromes at all, undoubted signs of acute meningitis suddenly appear. The cerebro-spinal fluid is under hypertension, clear in colour, and does not contain the typhoid bacillus, which alone can furnish a diagnosis.

It is only the special course of the disease which indicates its typhoid origin. In a few days, when the meningeal symptoms have disappeared, the more typical symptoms of typhoid fever appear, viz. the typhoid facies, the caked tongue, lenticular rose spots, etc. In exceptional cases at the onset, in the course of the disease or in convalescence, one may find meningitis produced by the germs of secondary infection, either alone or in association with the typhoid bacillus, such as the staphylococcus (Sergent and Lemaire, Giraudet, Breton), the pneumococcus alone (Dervitte, Sacquépée), or associated with the typhoid bacillus (Vincent), the tubercle bacillus (Chantemesse and Ramond, Comby), and the streptococcus (Vaillard and Vincent). There is nothing to distinguish them from suppurative meningitis. They are always fatal.

Special Senses

Organ of vision.—The patients often complain of a sensation of dazzling; often they close their lids as if they had photophobia. Jenner and Gairdner have noted a dilatation of the pupils which contrasts with the contraction of the pupils seen in typhus. Contracted pupils may, however, be found in typhoid fever also.

Keratomalacia and necrosis of the cornea have been noted (Trousseau), and also phlebitis with

phlegmon of the eye and orbit, irido-choroiditis, chorio-retinitis, etc.

Organ of hearing.—Patients complain from the beginning of the disease of *buzzing* and ringing in the ears. They may present *hardness of hearing* and even *deafness*, which is usually bilateral, without lesions of the ear, which suggests a central origin. *Suppurative otitis media* is not uncommon, and may cause in severe cases absolute destruction of the tympanum and loss of the ossicles. Every degree of deafness may be observed after these attacks of otitis.

Liver and Gall Bladder

Modern researches have established experimentally the theory of *descending infection* as opposed to the theory of *ascending infection*, to explain infective icterus.

The initial phenomenon is septicæmia, which is observed during the incubation period before the appearance of any obvious clinical sign. The intestinal lesion, which may be absent, should be merely regarded as one of the localisations of the typhoid bacillus, like the other lesions.

Experiments on animals and surgical operations on the human gall-bladder during life have shown the special localisation of the typhoid bacilli in the gall-bladder.

This localisation is usually accompanied by hepatitis and catarrhal angiocholecystitis, which at their onset have no clinical symptoms. In the course of typhoid fever one may observe suppurative cholecystitis, diffuse hepatitis and even hepatic abscesses containing the typhoid bacillus.

Some typhoid infections resemble relapsing jaundice. The infectious jaundice merely indicates the localisation in the liver.

Mild primary infective jaundice and catarrhal jaundice are the terms applied to different degrees of the typhoid infection. Chauffard, in particular, has contributed

to establishing this identity from a study of epidemics of jaundice contracted at the same source, and in which the jaundice may assume every clinical variety, including even icterus gravis. *Mild icterus*, which appears towards the third or fourth week, is of transient duration, and is accompanied by some tenderness and swelling of the liver, the stools retaining their colour.

Infective jaundice of moderate intensity is accompanied by more alarming symptoms.

"The onset is usually sudden; the patient is seized with shivering and fever, he complains of pains in the back and limbs, giddiness and headache, which is sometimes intense; digestive disturbance is constant, the tongue coated, anorexia absolute and vomiting frequent; there is a bilious diarrhœa which is usually profuse, and the temperature fluctuates between 100·4° and 104° F.

"The urine is scanty, dark and albuminous. The liver and spleen are often enlarged" (Gilbert and Fournier). The jaundice is intense, but the stools are not clay-coloured. In a few days improvement sets in and the jaundice gradually disappears.

Lastly, we may meet with grave *infective jaundice*, which ends in coma within a few days.

The typhoid state is intense, the jaundice is very marked at the onset and becomes progressively less. There are vomiting, erythemata, hæmorrhages, delirium, mental confusion, and high temperature with a more or less pronounced and persistent fall. "In these forms there is an association of the two anatomo-clinical syndromes, acute angiocholitis and hepatic insufficiency, but the two syndromes do not run parallel in their intensity" (Laignel-Lavastine).

Cholecystitis is not uncommon. It may be early (from the eighth to the eighteenth day) or late (from the twenty-ninth to the fifty-seventh day, or even longer still, after defervescence). In the first case it does not in any way affect the temperature curve; in the second case a slight and transient rise of temperature is sometimes noted.

Jaundice is exceptional. Pain is spontaneous or caused by pressure over the gall bladder, and is accompanied by muscular resistance localised in the right hypochondrium. To investigate this sign, which is present at the onset and at the height of the disease in every case of typhoid fever (Chauffard, Nobécourt, Paisseau and Marinier), the doctor should be on the right side of the patient's bed and pass his left hand backwards along the lower border of the ribs, so as to make the liver project forwards. The right hand should now depress the abdominal wall gently and progressively on to the gall bladder until the patient complains of a more or less sharp pain. This sign lasts until the beginning of convalescence. Its persistence after the temperature has fallen should make one fear a relapse (Radulesco and Atanassiu). In addition to this sign of tenderness of the gall bladder, we should note the *impaired resonance at the right base* which, according to Lesieur, is to be found by light percussion of the right base of the thorax. The upward enlargement of the liver is responsible for this impaired resonance. It is present in 80 to 90 per cent. of the cases and occurs earlier than the rose spots, serum reaction, enlargement of the spleen and diarrhœa. It diminishes and disappears in defervescence. Its return during convalescence indicates the onset of a relapse.

Hepatic abscesses in typhoid fever appear about the fourth or fifth week and are revealed by shivering, fever, grave general condition, meteorism and pain localised in the right hypochondrium in the region of the last costal cartilages. The liver is large and painful. The disease may run an acute, sub-acute or chronic course, and terminates fatally when the abscesses are multiple, or by opening into the intestine, peritoneum or lung when the abscess is big.

Peritoneum

Peritonitis in typhoid fever may originate from lesions of the spleen, liver and gall-gladder, etc.,

but the most frequent cause is perforation of the intestine.

We have already studied intestinal perforation and the peritonitis which results therefrom. Although it has been disputed by Dieulafoy, there is no doubt that inflammation may be propagated by continuity from the mucous to the peritoneal coat of the bowel without any perforation (Trousseau). In such cases the starting-point of peritonitis by propagation is to be found in a whitish, more or less adherent exudation on the non-ulcerated peritoneal surface, corresponding to a Peyer's patch.

This form of peritonitis has no special clinical symptoms.

Urinary System

Kidney.—Nephritis is fairly frequent in typhoid fever. Murchison says that he found it in 25 per cent. of his cases; Griesinger noted it in a third of his cases; Gubler and A. Robin state that it is *always* present. As a rule, the only symptom is the presence of *albumin* in the urine (at least, in the mild or moderate cases), apart from complications. It appears at dates varying from the first week to the middle of the third. The date of onset, amount and duration appear to be related to the severity of the disease. As a rule, it disappears in defervescence, but may persist and be the sign of a chronic renal lesion.

Robin has described a "renal form of typhoid fever" with the following clinical signs: slight diarrhœa, great prostration, adynamia, earthy pallor of the skin, lumbar pain, dyspnœa, profuse epistaxis, early cerebral phenomena, very high temperature, with great liability to chill, and extreme gravity. There is also a primary acute hæmorrhagic nephritis due to the typhoid bacillus, and some forms of acute non-hæmorrhagic nephritis may be due to the same cause.

Typhoid nephritis is very rarely associated with œdema and anasarca.

Convulsions of uræmic origin are also rare.

Bladder.—Relaxation of the sphincters with *involuntary emission of urine, and retention* necessitating the use of a catheter, have been noted.

Cases of cystitis manifested by pyuria in which the typhoid bacillus was present have been reported (Vincent, Lévi and Lemierre). A less frequent occurrence is a vesical syndrome of mild degree, characterised by frequent and painful micturition, a feeling of weight in the bladder, tenesmus and slight hæmaturia. These symptoms may disappear in a few days, but the pyuria may persist, and bacteriuria may outlast pyuria.

The urine in typhoid fever.—The quantity of urine passed by the typhoid patient (1) diminishes during the height of the disease; (2) increases slowly and progressively during defervescence; (3) is abundant at the onset of convalescence. This polyuria has received the name of "urinary crisis."

The physical characters, density and reaction of the urine vary with the quantity passed. At the height of the disease it is the colour of beef-tea with green, red or brown reflections (Gubler and Robin). Its specific gravity is 1015–1030 and more. It is extremely acid. On defervescence the specific gravity falls to 1017–1019, and even to 1005–1003 at the time of the urinary crisis.

The urine becomes paler and clearer as it gets more abundant. Its acidity may diminish until it becomes alkaline.

Urea increases during the first week (28, 57, 62, 78 grammes according to certain authors); it diminishes during the height of the disease, but remains above normal and becomes subnormal in convalescence.

Uric acid increases in the febrile period. From the normal 0·40 it may increase to 7·30 grammes on the seventeenth day (H. Jones).

It then decreases and falls below normal in convalescence. The *chlorides* passed in the urine may be reduced to a mere trace (Murchison).

Laubry thinks that there are periods of retention,

alternating with small discharges, which precede the abundant discharge of chlorides in convalescence. According to this writer, the chloride crisis at the end of typhoid fever may occur in one of three ways—

1. A sudden and complete discharge (20 grammes per day for several days).

2. An isolated and ephemeral discharge, followed by a very short retention or by a slow and progressive return of the chlorides to normal.

3. A slow and continuous discharge, which sometimes does not occur till ordinary diet is resumed.

The *phosphates* and *sulphates* may be slightly diminished.

There is no infection with intestinal lesions in which so much urinary *indican* is found as typhoid fever. *Leucin* and *tyrosin* are most likely to be found in severe cases. *Creatinin* is never absent.

The *urinary toxicity* is increased (Roques and Weil). From the prognostic point of view the chloride crisis alone appears to be of significance; a sudden discharge indicates a convalescence with normal evolution, while a slow discharge may indicate a relapse.

Diazo-Reaction

The diazo-reaction, as a colour test for the urine, has long been regarded as specific for typhoid fever.

Further investigations by several authors have shown that it is present in several febrile diseases, *e. g.* measles, pneumonia, scarlet fever and erysipelas. In typhoid fever it appears from the second to the sixth day, and lasts till the fifteenth to the twentieth day, according to the case, gradually losing its intensity.

It reappears with fresh rises of temperature, and up to a certain point its intensity is parallel with the fever.

The reaction has undergone certain modifications. The following method is much more delicate than the original one and often gives immediate results.

Reagents.

1. Paramidoacetophenol 0 gramme 50
   Concentrated HCl 50 grammes
   Dissolve and add
   Aq. destill q.s. 1000 c.m^3
2. Sodium Nitrite 0 gramme 50
   Distilled water 1000 c.m.^{3}

The urine to be examined should have been passed very recently, for the reaction disappears in a few hours after micturition.

Pour 10 c.c. of solution (1) into a long test tube and mix with four drops of the nitrite solution (2), and then add 10 c.c. of urine. Shake, make alkaline with 3 c.c. of ammonia and shake again vigorously. A positive reaction is shown by the scarlet red colour of the *froth*.

The Moriz-Weiss reaction with permanganate of potash has even less value than the diazo-reaction.

Various Glands and Systems

Salivary glands.—The salivary secretion is usually diminished, sometimes even almost completely suppressed. A few cases, however, of veritable sialorrhœa are on record (Merklen and Milhit).

Parotitis may be a sequela of adynamic and prolonged attacks. It is usually suppurative, and complicated with sloughing and extensive sinuses. The prognosis is grave.

The *pancreas* and *thyroid gland* may be the seat of more or less severe inflammatory lesions.

Testicle.—Patients aged from sixteen to thirty, in convalescence from an attack of moderate severity, may suddenly develop orchitis, either alone or in association with epididymitis, or epididymitis alone.

The symptoms are those of the orchitis of mumps, an effusion into the tunica vaginalis being exceptional.

The complication lasts about twelve days on the

average (Ollivier), but may be much longer. Suppuration may occur.

The typhoid bacillus has been isolated in these cases (Vincent).

Female genital organs.—Inflammatory swelling of the labia majora, ending in suppuration, vulvitis, Bartholinitis, retro- or peri-uterine hæmatocele, and a more or less severe gangrene of the vulva have been recorded.

These complications are rare and late events, and may pass unnoticed. Driout and Duplant saw an ovarian cyst, which had been present for several years, suppurate in the course of typhoid fever. The pus was very abundant (10 litres), and contained the typhoid bacillus.

Lymphatic glands.—All the lymphatic glands are affected in typhoid fever, including the mesenteric, or extra-mesenteric, cervical, lumbar, inguinal, bronchial, etc.

The inflammation generally subsides fairly quickly. It is to its presence and persistence that we may attribute the paroxysmal cough, resembling pertussis, that may be observed in convalescence.

Suprarenal capsules.—According to E. Sergent the typhoid state presents certain symptoms, such as depression, prostration and hypotension, indicating *suprarenal insufficiency*, which in an aggravated form characterises the severe varieties of the disease, especially the adynamic and cardiac forms.

Acute suprarenal insufficiency may be manifested by a fall of the temperature and arterial pressure, bilious and greenish vomiting, profound prostration, and pain in the lumbar region which may simulate peritonitis.

The presence of suprarenal insufficiency may be detected by means of the *white line*, and above all by the result of treatment.

If the finger or a blunt object be drawn over the surface of the skin of the abdomen without exercising any pressure, in thirty to sixty seconds a white line is seen to appear, its width being greater than the blunt

object which caused it, and lasting from two to five minutes and even more, and never accompanied on each side by a pink line.

This is Sergent's suprarenal white line, which is the converse of the meningeal red streak, and may be regarded as a reflex spasm of the capillaries.

The suprarenal origin of this symptom appears to find a definite proof in the fact that adrenalin administered therapeutically causes the hypotension and the white line to disappear simultaneously. The therapeutic proof is without danger even in the course of acute peritonitis, and cannot fail to be of value both as a guide to diagnosis and as a remedy for the cardio-vascular asthenia.

Muscular System

The pathological anatomy of *typhoid myositis* is now well known, but its clinical signs are still indefinite. We are acquainted only with the lesions which result from it, such as muscular rupture, hæmorrhage and abscesses.

Muscular rupture is seen at the end of the third week or in convalescence.

It may be the result of a very slight effort (coughing, sneezing, etc.).

It occurs in order of frequency in the adductors and psoas, rectus abdominis and pectoralis minor, transversalis, muscles of the shoulders and the gastrocnemii.

It may pass unnoticed or be revealed by a sharp and sudden pain.

Hæmorrhage which follows rupture has no symptoms if it is deep and slight in amount; if superficial it is indicated by an ecchymosis.

When it is very profuse it may give rise to a soft and fluctuating hæmatoma, with or without an ecchymosis.

As a rule, the rupture and hæmorrhage clear up uneventfully, but the lesions may suppurate, as will be seen by local redness of the skin and fluctuation, as well as by a slight rise of temperature.

Osseous System

The irritation of the bony tissue in typhoid fever is revealed by exaggerated *growth* and the *lineæ albicantes*, due to elongation of the skin, which are seen in young patients when they leave their bed. But the most interesting phenomenon is the osteo-periostitis of convalescence (Chassaignac and Maisonneuve, Keen), which is chiefly met with in those patients whose osseous system has not yet attained its full development (Hutinel).

It is often multiple and symmetrical, and may affect any bone, but has a predilection for the long bones, especially the tibia.

Hutinel classifies the lesions of the periosteum as follows—

1. *Circumscribed periostitis.*—This is the most frequent form, but has attracted least attention because the symptoms are indefinite, of short duration, and complete recovery takes place.

2. *Osteo-periostitis ending in abscess formation.*—Fever, swelling of the bone at a definite spot, and redness and swelling of the skin, which gives passage to pus from a limited sub-periosteal abscess, either spontaneously or after incision.

This form always ends in recovery, but may last a very long time owing to the presence of sinuses and sequestra.

3. *Chronic periostitis* with gradual onset, resulting in deformity of the bone.

Pyæmic arthritis may affect the joints, constituting a primary localisation of the typhoid bacillus, but no special description of the symptoms is needed.

Polyarticular arthritis may also occur. Its very painful character and appearance at the onset of typhoid fever may cause it to be mistaken for acute articular rheumatism.

Lastly, *monoarticular arthritis* localised in the knee or hip is fairly frequent and is revealed by puffiness, swelling and pain, which end in recovery, ankylosis or spontaneous dislocation.

Skin

The skin of the typhoid patient is *warm* and *dry*. In the early hours of the morning it becomes damp and covered with *perspiration*.

In defervescence profuse sweats occur which have been called critical. Forms of typhoid fever have been observed in which the perspiration was so profuse that they were called "sweating fevers" (Borelli, Jaccoud). Perhaps these peculiar forms, which are so frequent in Southern Italy, result from an association with malaria, or are they really to be regarded as due to an infection by the *micrococcus melitensis ?*

The palms and soles present a saffron-yellow colour (Filipowicz), but this is also found in other diseases. This *palmo-plantar sign*, as it is called, may be followed by *desquamation* of these regions in convalescence.

The desquamation may be more general and extend to all parts of the body, especially in young subjects (Roger). The hair often falls out.

Eruptions.—Various eruptions are met with in typhoid fever. One of them may be regarded as a specific clinical symptom, viz. the lenticular rose spots of Louis. The others are of secondary importance.

According to Murchison, the *lenticular rose spots* have a rose or pink colour, but which varies slightly in tint according to that of the patient's skin. Their form is rounded and regular, their margin is well-defined, and they measure from half a line to two lines in diameter. When the point of the finger is passed gently over the skin, each spot can in most cases be felt to be slightly elevated above the surface. Their outline is rounded or convex, but not acuminated. They are never indurated; but, in rare cases, a minute vesicle may be discovered at their apex. They are never converted into petechiæ; but during the whole period of their existence they disappear completely on pressure, and return when the pressure is removed.

The seat of election for the typhoid exanthem is

the thorax, abdomen, axillæ and sometimes the root of the thighs. Murchison often found them on the back, when they were not present anywhere else, and he occasionally noted that they were larger and more numerous on the back than on the front. The spots are developed in large numbers after a warm bath (Louis, Jenner).

In most cases the eruption appears on the seventh or eighth day. Exceptionally it is noted after the twentieth day (twentieth and thirtieth days according to Louis, and forty-fifth and fifty-second according to Rilliet and Barthez). After the fall of the temperature it is a premonitory symptom of a relapse.

An early appearance, before the seventh day, is as rare as a late eruption, and seems to be an accompaniment of severe and exceedingly acute forms.

The eruption is, as a rule, discrete. The spots are not very numerous at once; they appear, without any order, in successive crops, in groups of three or four, and then disappear to give place to others. The average duration of each spot is from three to five days.

The eruption lasts five to seventeen days, ten on the average. There are spots, however, which persist abnormally for ten, fifteen and even twenty days, and leave, on fading, a dark deposit of pigment or copper-coloured macule. In those cases in which there was a minute vesicle in the centre of the spot, a slight desquamation occurs at the former site of the vesicle. Certain spots are transient and disappear in one or two hours. As a rule, they are not numerous (ten to twenty at a time), and in some cases they are rarer still. It may be possible to find only three or four, or even less.

Occasionally the eruption may be so profuse as to imitate the exanthem of measles.

In subjects with a white and fine skin the lenticular eruption is sometimes preceded by a hyperæmia which sometimes produces a continuous redness, and some-

times a punctate rash limited to a narrow portion of the integument. In such cases it may be mistaken for scarlatina.

In severe forms the spot changes its tint and grows paler as the adynamia increases. A similar phenomenon occurs at the moment of death. Not only is the eruption never to be found on the corpse, but, in a patient who succumbed when the rash was fully developed, the eruption disappeared in a few hours before the terminal collapse (Cheurlot). The eruption is never completely absent. In cases in which no lenticular rose spots have been found, they may possibly have escaped notice for various reasons, *e. g.* small number, transient duration, unusual site, peculiar colour of the skin, unusually early or late development, etc.

Other eruptions may be found in typhoid fever, *e. g. purpura*, which is always of grave prognosis, and *erythemata, mild* or *severe.*

In addition to the eruption, which may be polymorphous, morbilliform or scarlatiniform, the severe cases are characterised by a grave adynamic general condition, a fall of temperature with re-ascent, vomiting of greenish fluid, green and fœtid diarrhœa, and ulcerations of the lips and nose. The prognosis is grave (a mortality of 60–80 per cent.).

The well-known pearly vesicles called *sudamina* are very common. They are situated on the front of the thorax, on the abdomen, neck and axillary regions. They may be more or less confluent, but, as a rule, are fairly discrete.

Gangrene of the skin is fairly frequent. It usually occurs in those parts of the body which are for long subjected to continuous pressure. Examples are seen in the sloughing of the skin over the sacrum and ischium, elbows, heels and scapulæ. They are not so frequent as formerly. They occur at the end of the second week, or in the third or fourth in severe attacks, or in subjects, exhausted by hæmorrhage or profuse diarrhœa, who *have not received proper attention.* They may be the starting-point of many more or less severe

complications such as multiple abscesses, gangrene, erysipelas, etc.

In addition to the serious *typhoid pyœmia*, writers have recorded cases of *furunculosis* and *subcutaneous abscesses* succeeding one another in large numbers for a long period so as to resemble glanders (Lailler).

CHAPTER III

CLINICAL CHARACTERS OF PARATYPHOID FEVERS A AND B

In spite of the similarity of their clinical symptoms, and even of their anatomical lesions, paratyphoid fevers constitute morbid entities quite distinct from typhoid fever. An attack of typhoid fever does not confer immunity against an attack of paratyphoid fever, or vice versa. Since the important investigations of Achard and Bensaude in 1896, the clinical and bacteriological history of paratyphoid infection has grown considerably. The paratyphoid A and B bacilli, like the typhoid bacillus, are able to produce not only general infections of a septicæmic type, but also infections which are localised from the first. Belonging to the same family of bacteria as the typhoid bacillus, but nevertheless differing from it, the paratyphoid bacilli play a similar rôle to the typhoid bacilli in infections of the liver and bile ducts. The ordinary clinical forms of paratyphoid A and B resemble those of typhoid fever, and it is always by comparison with the latter that a diagnosis has hitherto been made. It was held that paratyphoid fevers in the great majority of cases assumed an attenuated "typhoid" form.

Paratyphoid fevers, which had been comparatively rare in France before the present war, have since become very frequent, especially since August 1915.

As accurate diagnosis became more frequent by discovery of the specific infective agent, it was realised that paratyphoid fevers had usurped their reputation for benignity, which was perhaps due to a purely clinical diagnosis.

At the present time it is agreed that paratyphoid fevers A and B may assume all the symptoms of typhoid fever and realise every clinical type. They may even present the same complications, which, though possibly less frequent in paratyphoid fevers, are equally severe.[1]

For this reason it would be difficult to give here any clinical signs which in themselves would be sufficient to allow an exact diagnosis to be made between typhoid fever and paratyphoid fevers A and B. This diagnosis the laboratory alone can establish undoubtedly by means of an early blood-culture.

The *incubation period* in paratyphoid fevers varies considerably; on the average it is from nine to fifteen days, but it is sometimes shorter, and may be reduced to five or six days (Sacquépée), four to five (Dibos), or three to eight (Lenglet).

The phenomena of onset resemble those of typhoid fever of a mild form, viz. great lassitude, insomnia, headache, epistaxis, nausea, anorexia, thirst, pain in the back, orbits and nape of the neck, cramps in the calves, etc.

Shivering has been noted as fairly constant at this period (H. Vincent, Job, Robinson), and is sometimes repeated for several days. Constipation is very frequent (Sacquépée, Chevrel), but diarrhœa is not rare (Meslay and Coville, Job), being met with in about one out of two cases (Lenglet, Coyon and Rivet, etc.). Boidin and Burnet judiciously remark that "in the course of this war paratyphoid fevers have often supervened in cases of prolonged diarrhœa which have lasted three or four weeks without fever."

The stools in paratyphoid usually have a putrid odour (Job) and a more or less ochre colour; they contain greyish fragments of desquamated and putrefied intestinal mucosa (H. Vincent). They do not leave the

[1] It will be remembered that the lesions found at autopsy may be identical in paratyphoid fevers and typhoid fever. Ulceration of Peyer's patches and perforative peritonitis, however, are less frequent in paratyphoid fevers A and B.

same coloured stains on the sheet and bed linen as the typhoid stools (Landouzy).

The onset of paratyphoid fevers is often slow and progressive (Boidin and Burnet, Coyon and Rivet, Robinson, Grenet and Fortineau, Netter and Ribadeau-Dumas, etc.). But, more frequently still, it may be sudden, with shivering and vomiting which mark the onset of the infection (Grenet and Fortineau, Chevrel, Job, Rathery, etc.).

The patient may then fix the exact moment at which he noticed the first symptom.

In three or four days the temperature reaches its maximum, which is about 104° F. (Job, Lévi-Valensi, Netter and Ribadeau-Dumas, Chevrel, etc.). Vomiting is frequent, the patient may not be able to keep anything in his stomach. Severe headache, pain in the back, and *occipital pain*, which may even precede the febrile symptoms, have been noted as fairly common during this initial period. Sometimes the onset may be dramatic and simulate meningitis (Job, Netter and Ribadeau-Dumas), or appendicitis (Grenet and Fortineau), and be accompanied by extreme prostration, by convulsions in children, and by vomiting at all ages (Job, Robinson, etc.). The patient very soon begins to resemble a case of typhoid fever of the end of the first week. He preserves the congestion of the cheeks and conjunctivæ noted by Murchison as one of the symptoms of typhoid fever. The tongue is dry and coated, the gums are covered with a pultaceous deposit, and the throat is red. Labial, facial and buccal herpes is frequently observed (Vincent, Aubry, Job, Chevrel): some writers, however, have seldom met with it (Coyon and Rivet). *Sore throat* is not exceptional. Duguet's *ulcerations* have been found. At the onset of the disease the patient fairly often suffers from colic and *diffuse abdominal pain* on pressure, without special localisation in the right iliac fossa (Vincent). This pain may last for one or several days. Sometimes pain and *gurgling* have been noticed in the right iliac fossa (Netter and Ribadeau-Dumas, Robinson). Jacquement

states that "complete absence of pain or tenderness in the right iliac fossa should make one think of paratyphoid conditions." The *abdomen* is sometimes distended. The *liver* is almost always increased in size, and sometimes to a degree rarely observed in typhoid fever (Chevrel). The *spleen* is less big than in typhoid fever (Landouzy), whereas, according to other writers, it is always much enlarged (Job, Meslay and Coville, Chevrel), so that its edge can be felt several fingers' breadths below the false ribs (Aubry).

Sweating is frequent and sometimes profuse, occurring late in the evening or in the night.

The *lenticular rose spots* which Landouzy regards as inconstant are present in 60 per cent. of the cases (Robinson). They may be rare, or, on the contrary, remarkably plentiful, appearing in successive crops, sometimes involving the face (Chevrel), and extending over the neck, cheeks, arms, forearms, and leaving only a few small areas of healthy skin (Grenet and Fortineau).

In several cases a *buccal enanthem* has been found (Grenet and Fortineau, Petges, Dumora and Peyri). The rose spots sometimes assume the papular type (Meslay and Coville), which is rare in typhoid fever. They may be large and of short duration (René Benard). Their colour is sometimes dark or violet pink, with, occasionally, a central point in which the colour is more pronounced (Lenglet). They have been seen to appear after complete fall of the temperature (Chevrel), and to last for several days during apyrexia (Vincent).

The *typhoid state* is usually ill-marked (Job, Landouzy, Boidin and Burnet, Coyon and Rivet, etc.). Some have found more pronounced *nervous symptoms* than in typhoid fever, whereas, according to others, these symptoms are either absent or ill-marked (Étienne, Jeandelize and Soncourt). Ataxo-adynamic forms, however, are not exceptional. Cases have been observed of hemiplegia with sensory troubles, without aphasia, psychosis of the mental confusion type with

oneiric delirium (Raymond, Parisot and Orticoni), psychoses with post-oneiric ideas (Merklen), sphincter troubles; retention or incontinence of urine, incontinence of fæces (Merklen), neuritis of the vagus, paresis of the deltoid, diminution of the reflexes, ankle clonus and acute encephalitis (Job). The *urine* is scanty and dark. Albuminuria is present in half the cases (Aubry), but is slight and of short duration (Job, Raymond, Parisot and Orticoni).

According to Aubry, the *diazo-reaction* is generally absent; whereas, according to others, it is fairly frequently positive.

The pulmonary signs are very slight; mild bronchitis is merely found in most of the cases (Chevrel, Aubry).

In soldiers, in the course of this war, there have generally been found congestion of the bases, acute or prolonged in character, congestion of the apex, simulating tuberculosis, in which the patient expectorates numerous paratyphoid bacilli in the sputum, pleuro-pulmonary congestion, broncho-pneumonia (Raymond, Parisot and Orticoni), and pneumonia with splenization (Minet). The hæmatological formula does not differ from that of typhoid fever.

It was generally thought that the heart was rarely affected in paratyphoid, and that one could only find bradycardia and extra-cardiac murmurs, and never tachycardia. J. Minet, in 19 out of 60 cases, observed more or less marked myocardial manifestations.

He found the same clinical types as in typhoid myocarditis—

(1) *Latent forms*, most frequently met with, in which affection of the myocardium was revealed only by examination of the heart and pulse.

(2) *Grave forms*, in which disturbance of the circulation indicated the failure of the cardiac muscle.

(3) *Syncopal forms*, rare, in which sudden death might be the first and only symptom.

(4) *Chronic forms*, also rare, following the acute phenomena.

In 7 out of 19 cases this author found tachycardia,

and in 11 out of 19 embryocardia. In this connection he remarks that fœtal rhythm, which is of grave prognosis in the typhoid patient, has not the same significance when it appears *as the only cardiac sign* in paratyphoid fever. It assumes the character of a grave sign only when it is accompanied by other indications of cardiac failure.

The *temperature* rarely exceeds 104° in the ordinary

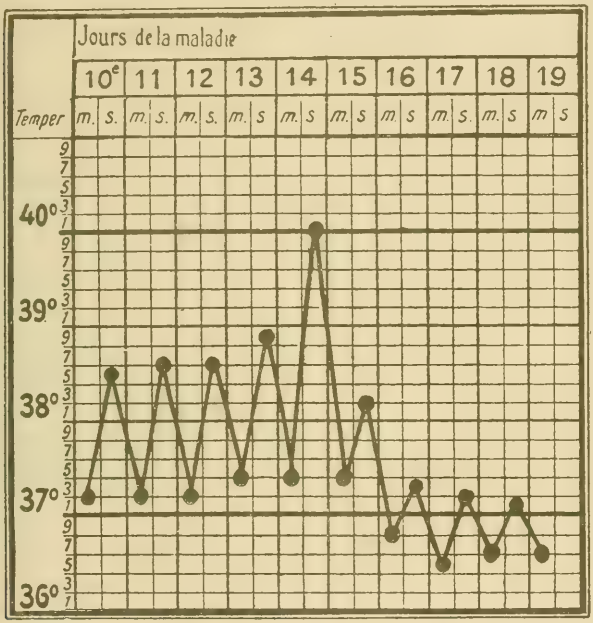


FIG. 8.—Boy, aged 13½. Paratyphoid fever A.

forms. Its curve may be exactly like that of typhoid fever with a period of ascending oscillations. But, as a rule, the fastigium is reached in two or three days. The height of the disease is often of very short duration. In eight or ten days (Job), or seven to fifteen (J. Lévy-Valensi), the temperature falls to normal by lysis. This return may be more rapid still, taking only two or three days (Aubry).

In such cases the temperature curve does not show a plateau. Sometimes, however, the plateau is present,

and in severe cases may be as high as 102·2° or 104·0°, sometimes it keeps about 100·4°.

Shortened forms of paratyphoid fever are to be met with, which probably include a certain number of the cases which were formerly described as febrile gastric derangement, or gastric fever.

The *pulse* closely follows the temperature. Its maximum varies, on the average, from 80 to 100, or 120. As a rule, it appears to undergo a marked slowing in the period of apyrexia, falling to 60 beats in the minute, and often less—52, 48, 34 (J. Lévy-Valensi).

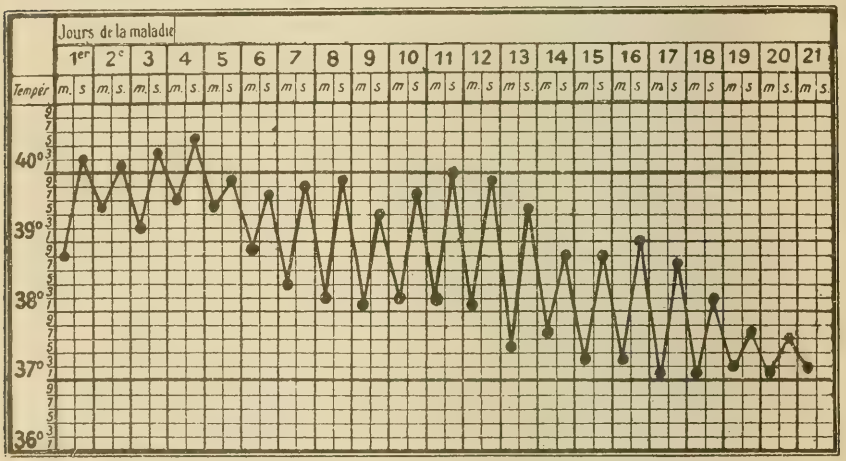


FIG. 9.—Girl, aged 12½. Paratyphoid fever B.

Generally speaking, the pulse appears to be slower than in typhoid fever (Robinson). Dicrotism, also, appears to be rarer.

The course of paratyphoid fever is shorter than that of typhoid, and, as a rule, its total duration is less than a fortnight (Chevrel, Meslay and Coville, Robinson, Dévé, Job). But, according to certain authors, it may be as long—three to four weeks, on the average, rarely less, but often longer, according to Aubry, Coyon and Rivet.[1]

[1] According to Merklen and Trotain, the duration of the disease is in relation to the age of the patient: twenty-four to twenty-seven days for the ages twenty to thirty, and twenty-seven to thirty-two days for the ages thirty-one to forty-six.

Netter and Ribadeau-Dumas have recorded cases in which the temperature did not become normal until after more than three months.

These cases are not exceptional. During this long period it seems, as these writers say, that there is a succession of several attacks. These may follow so closely one upon the other that there cannot be a question of relapses; or, on the other hand, several days of normal temperature may intervene between the attacks.

Relapses are found to be as frequent as in typhoid fever (10 per cent., according to Rimbaud; more

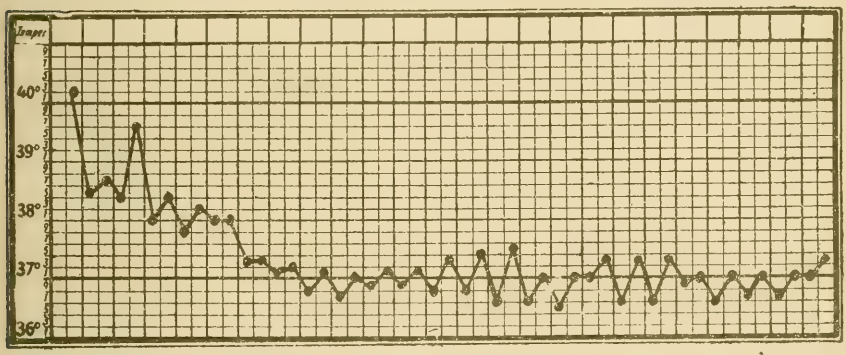


FIG. 10.—Mild paratyphoid fever B. Positive blood culture. (Rathery.)

frequent still, according to Grenet and Fortineau). According to Job, recrudescences are more frequent than relapses.

The onset of convalescence is frequently marked by polyuria.

The hypothermic phenomena are rarely so marked as those preceding the termination of typhoid fever, but sometimes the amphibolic stage is much more pronounced, especially in paratyphoid A (Coyon and Rivet). It was for a long time thought that the course of paratyphoid fevers was mild, and that complications were exceptional. But it has been found that in war time these diseases fairly frequently present grave and complicated forms.

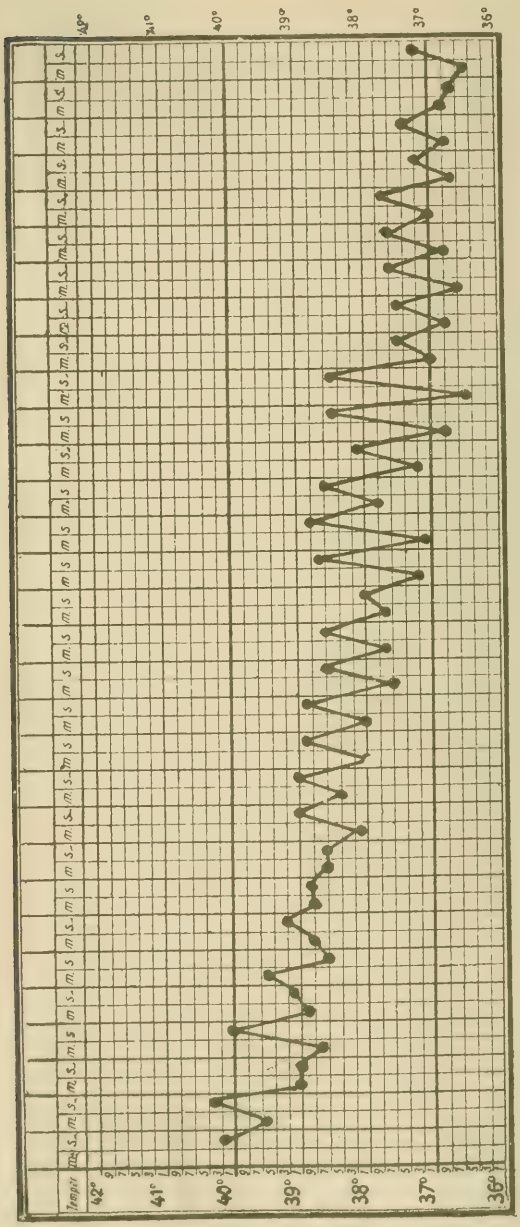


Fig. 11.—Paratyphoid fever B. Positive blood culture. (Rathery.)

The adynamic form is fairly frequent, especially in paratyphoid A (Boidin and Burnet). But an ataxo-adynamic form of paratyphoid B has also been observed.

Intestinal hæmorrhage is not rare, being accompanied by alarming symptoms such as fainting attacks, cold sweats, feeble pulse, etc. It may recur for several days in succession, or reappear after an interval of a fortnight (J. Minet). It seems to be less severe than in typhoid fever, but it may be fatal. It is observed in 5 or 6 per cent. of the cases.

Coyon and Rivet, in a case of paratyphoid B diagnosed by a blood-culture, noted a case of death after twelve days of peritoneal

symptoms. It was an instance of *peritonitis without perforation.*

Félix Ramond and Schultz published a similar case, which occurred on the 15th day of paratyphoid A, which had been diagnosed by a blood-culture and appeared to be a mild case. The patient died after peritoneal symptoms lasting for seven days, a fall of temperature to 97·4°, painful and retracted abdomen, diminution of the urine, and a pulse of 100. No blood in the stools. Median laparotomy. Death from cardiac collapse. No perforation. Collection of pus in the right flank. Bourges has observed *intestinal perforation* occurring insidiously in paratyphoid, and without any of the ordinary symptoms of peritonitis. Grenier, Hornus in Morocco, Raymond, Parisot and Orticoni have also seen cases in the course of paratyphoid A and B.

Raymond, Parisot and Orticoni have noted the great frequency of *phlebitis.* They found seventeen cases in the left lower limb, seven in the right lower limb, and one in the left brachial vein. Death occurred after broncho-pneumonia from a suppurative infarct; the starting-point was a thrombus in the right iliac vein. J. Minet has seen two cases of phlebitis, one in the femoral and one in the brachial vein.

The kidneys and bladder may be severely affected. Cases of extremely abundant albuminuria in paratyphoid A, and of hæmaturia in paratyphoid B, have been reported by Raymond, Parisot and Orticoni.

The respiratory system may be the seat of grave complications.

Giroux noted, in the course of paratyphoid A, a pleurisy which was at first serous and later purulent and hæmorrhagic. Pleuro-pulmonary congestion of protracted course is fairly frequent, with an effusion containing neutrophil polymorphonuclears.

E. Joltrain and G. Petitjean had the opportunity of seeing nineteen cases of pleurisy among 310 cases of paratyphoid fever in soldiers (6 per cent.); eighteen were due to the paratyphoid B bacillus, and only one to the

paratyphoid A bacillus. Fifteen were sero-fibrinous, two were purulent, and two dry. As a rule they appeared in the course of latent or abortive forms, in which they were sometimes the first symptoms (pleuro-paratyphoid).

In addition to the complications affecting the nervous system already noted, we may mention a case of typical tetany which occurred in a patient on taking a warm bath. In childhood he had had repeated convulsions. He remained a subject of spasmophilia. Tetany was present in him potentially, and a general disease, such as typhoid fever, was sufficient to render it patent (Bedos, Babonneix and Corone).

Parotitis, simple or suppurative, is not extremely rare. Sabrazès has published a case of suppurative myositis of the right pectoralis major due to the paratyphoid A bacillus.

Catarrhal or suppurative otitis is fairly frequent, as well as suppurative lesions in the bones and joints. Lesions of the liver and gall-bladder (hepatalgia, hepatomegaly and angiocholecystitis), certain very painful forms of which seem to give rise to peritoneal symptoms, have been noted in 80 per cent., either in the course of the disease, or after the fall of the temperature, by Raymond, Parisot and Orticoni. Lastly, the same authors recorded a case of orchitis with suppuration in the tunica vaginalis, and Giroux had a case of orchi-epididymitis with suppuration and elimination of the affected testicle.

We can see by the foregoing description, first, how closely allied are paratyphoid fevers, by their symptoms and complications, to true typhoid fever; and, secondly, how we can only admit with reserve the mild character hitherto attributed to the two paratyphoid fevers.

They are certainly less frequently fatal than typhoid fever. Statistics, however, confirm their degree of gravity during the war.

Merklen and Trottain diagnosed by blood-culture and treated 446 paratyphoid fevers, 356 of which belonged to type A, and 90 to type B.

They had fifteen deaths, ten of which occurred in paratyphoid A and five in paratyphoid B. The causes of death were the following: broncho-pulmonary complications, six cases; intestinal hæmorrhage and perforation, three cases; virulence of infection, icterus and parotitis, two cases; cardiac collapse, uræmia, meningitis, and diphtheria, one case each.

Grenet and Fortineau diagnosed by blood-culture seventy-six cases of paratyphoid A and twelve of paratyphoid B. They had three deaths, two in paratyphoid A from intestinal perforation and myocarditis, and one in paratyphoid B from intestinal perforation.

Dévé, in 201 positive blood-cultures, found 140 cases of paratyphoid A and sixty-one of paratyphoid B. His mortality was 0·7 per cent. for paratyphoid A and 1·6 per cent. for paratyphoid B.

These statistics, like those of Sacquépée, Burnet and Weissenbach, Leger, Abt and Dumont, Nobécourt and Peyre, and J. Carles, show that in the army in campaign paratyphoid A fevers are much more frequent than paratyphoid B. In certain regions, however, paratyphoid B has been predominant. The same statistics, as well as those of Benard, Dibos, etc., also prove that paratyphoid fever A is less severe than paratyphoid fever B. Before the war of 1914 paratyphoid fevers were extremely rare in the French army, in which doubtful cases were examined by a blood-culture.

As Prof. Landouzy remarks, complications, judging by the cases published, seemed exceptional, especially intestinal hæmorrhage and perforation. But the excessive predisposition which the war provoked for diseases of typhoid form, hæmorrhage and perforation in the course of this war have become as frequent as in typhoid fever. The first two statistics quoted above further show that out of 584 authenticated cases of paratyphoid, of which eighteen ended fatally, five deaths were due to *intestinal hæmorrhage* or *perforation*, a mortality of 0·93 per cent., and that these complications were present in more than a quarter of the fatal cases.

Among 170 cases of paratyphoid there were eight deaths. J. Carles had two deaths from intestinal hæmorrhage and one from perforation, *i.e.* more than a third of the deaths were due to these causes.

Paratyphoid fevers, however, include a number of attenuated forms which may pass unnoticed by the doctor, or even the patient. Prof. Landouzy has insisted on this point. "Many morbid episodes, hitherto described by nosographers as mild typhoid, mucous fever, febrile gastric derangement, are probably the result of infection by one of the paratyphoid bacilli." There are perhaps very few combatants who did not present these diminutive attacks of paratyphoid infection, in the form of colic, pains in the body and limbs, and fever, for a few days. It is not less probable that before the period of bacteriological diagnosis numerous pathological states described by the name of *typhoid fever* with sudden onset, or with abdominal, pleural or hepatic complications were really due to infection by the paratyphoid bacilli A and B.

The identity of the symptoms observed in these diseases—which constitute, nevertheless, distinct processes, and do not confer reciprocal immunity—easily explains the confusion. It may be said that without the aid of the laboratory the exact diagnosis of typhoid fever, or of paratyphoid fever A or B, cannot be established.

The same statement applies to bacillary or amœbic dysentery, meningococcal, parameningococcal or pneumococcal meningitis, and to diphtheria and pseudo-diphtheria.

The infected organism cannot, indeed, oppose an unlimited number of reactions to micro-organisms which are more or less related to one another, like the typhoid and paratyphoid bacilli. Besides this more or less severe typhoid form, with its features which we will summarise later, certain forms have been described which are peculiar to paratyphoid.

The *mild form*, which closely resembles *febrile gastric derangement*, is characterised by digestive troubles

such as anorexia, vomiting and diarrhœa, with a more or less intense febrile state. The onset is sudden and the course rapid. Discrete *lenticular rose spots* may be seen.

Some of these infections which bear only a distant resemblance to typhoid fever, except in the presence of rose spots, are so mild that it has not seemed necessary to the patient to stay in bed. They have received the name of "ambulatory paratyphoid" (Chevrel).

The *gastro-intestinal form*, which is usually due to intoxication of alimentary origin, presents variable symptoms according to the gravity of the infection. In these cases it is the paratyphoid B bacillus which is the cause, or the *Bacillus enteritidis*, which belongs to the same group of the Salmonelloses. The morphological, cultural and biological properties, as well as the pathological features of the Bacillus enteritidis are exactly those of the paratyphoid bacillus B, from which it can only be separated by its reaction towards agglutinating serums (Rieux and Sacquépée).

The symptoms due to these alimentary infections generally begin shortly after the suspected meal, on the average in twelve to thirty-six hours, sometimes sooner and sometimes later; the extreme limits are one hour and four days. In the same epidemic the incubation period may vary, according to the individual, from one or two hours to two days, but as a rule it is the same for all, so that one may witness a veritable explosion, which is often dramatic in its intensity. In very mild cases the patient has headache and diarrhœa, as well as some pains in the limbs, presents more or less marked asthenia, and sometimes shows a slight rise of temperature. Two or three days afterwards he is cured. If the attack is a little more severe, the preceding symptoms are a little more marked and accompanied by colic and vomiting. The stools are numerous, liquid, greenish, blackish or brownish in colour, and of very fœtid odour. Vomiting, which is at first alimentary, becomes bilious and sometimes bloody. The patient is obnubilated, sometimes pros-

trated. His temperature is not high, as a rule, but may reach 104·8° (Vagedes). All these symptoms vary in duration, lasting two, three or eight days, sometimes even a month or two, and even more.

Recovery is the rule, but even in mild cases convalescence is often protracted and tedious.

"When the attack is still more severe it almost always assumes the appearance of *cholera nostras*. The stools, which are often liquid and even of the rice-water character, occur ten to thirty times in the forty-four hours, and are accompanied by persistent vomiting; the small and rapid pulse, pallor of the face and anxiety, peripheral algidity and tendency to collapse, prostration and cramps, remind one of cholera; the temperature varies and is fairly often below normal" (Sacquépée).

In E. Sergent's case the resemblance with cholera was even more striking. After choleriform symptoms of the most alarming character for three days the temperature rose and kept between 103·2 and 103·6° F. for seven days. During the course of the intoxication the most abnormal symptoms may arise, such as myosis, conjugate deviation of the eyes (Tiberti), mydriasis, aphonia, incontinence of the anal sphincter, anuria, purpura (van Ermengem), *rose spots* (Cahn), herpes, etc.

Icterus is exceptional according to Curschmann, but frequent according to Audry, and is shown by pigmentation of the skin and urine, clay-coloured stools and increase in size of the liver and spleen.

Lastly, some forms resemble dysentery with tenesmus, colic and very numerous bloody stools (Jacobson).

The choleriform attacks usually run a fairly rapid course lasting a few days, rarely more than a week (Job, Audry).

In the course of the same epidemic these different forms may be seen in existence simultaneously.

In peace time the mortality is low. In a total of 2725 cases consisting of the most different types Sacquépée found only four deaths—a mortality of 1·5 per cent.

Persons who have had typhoid fever and who have been vaccinated against it are by no means immunised against the paratyphoid fevers A and B, but may contract paratyphoid fevers which run an ordinary course.

CHAPTER IV

DIAGNOSIS

It is of the utmost importance to make an early diagnosis in typhoid and paratyphoid fevers, both in the patient's interest so that treatment may be commenced as soon as possible, and in the interest of the community so that the necessary prophylactic measures may be taken.

We have already said that by unaided clinical observation only a presumption could be formed as to the existence of one or other of these affections. An exact differential diagnosis is only possible by the help of the laboratory. But this it may be impossible to obtain. We will, therefore, devote the first section of this chapter to a description of the principal rules for the clinical diagnosis of typhoid fever and paratyphoid fevers.

In the second section we will study the laboratory methods, which enable us to make a diagnosis by the isolation and identification of the causal agent of the infection or by the study of the specific humoral reactions produced in the organism by this agent.

I. Clinical Diagnosis.

At the onset the clinical symptoms which might guide the diagnosis are common to all infections. Individually they have only a very relative value, but collectively they gain in precision and may make one suspect typhoid fever. During the first week the diagnosis will be guided by the malaise, peculiar type of headache, insomnia, epistaxis, slight bronchitis, coated tongue,

or diarrhœa with special characters, pain on pressure in the epigastrium, or right iliac fossa, with gurgling, and fever with evening exacerbations which become more intense each evening.

If after a week of this state of affairs the spleen becomes enlarged and lenticular rose spots appear, there can be no doubt about typhoid fever, whatever the other symptoms may be (Homolle). A much more sudden onset, with a temperature of 103·2° F. on the second or third day, shivering, vomiting and the appearance of herpes, should make one think rather of paratyphoid A or B. In making a diagnosis at this period one should take into account the existence of an epidemic, the non-acclimatisation of the subject, his age and the life he has been leading, as well as his pathological antecedents (previous attack of typhoid or paratyphoid fevers).

At the height of the disease the gastro-intestinal symptoms, further increase in the size of the spleen, eruption of lenticular rose spots, but most of all the typhoid state, will be the principal elements in the diagnosis. These symptoms and their diagnostic value have been studied at length in a previous chapter.

There is no pathognomonic clinical feature in paratyphoid fevers, either to distinguish paratyphoid fever A from paratyphoid fever B, or to distinguish between paratyphoid fevers and typhoid fever properly so called.

Paratyphoid fevers may present all the symptoms and all the complications of typhoid fever. However, one may be guided in the diagnosis, though not constantly, by certain signs, among which the following are the most frequently observed—

(1) The suddenness of the onset, with vomiting and shivering.

(2) The frequency of pain in the occiput at the onset.

(3) The early eruption of labial, facial or buccal herpes.

(4) An ill-marked typhoid state.

(5) A fairly frequent meningeal reaction.

(6) Slight degree of diarrhœa, constipation the rule.

(7) Frequency and intensity of perspiration at the onset or in the course of the disease (paratyphoid fever A and B).

(8) The sometimes remarkable, though not invariable, abundance of lenticular rose spots, which may appear at the onset of defervescence and last for some days later.

(9) The frequent and considerable enlargement of the liver.

(10) Shorter course of the disease.

We must, however, insist on the fact that these symptoms are not constant, that they may exist separately, and that, finally, many of them have been found in genuine typhoid fever.

The only clinical character which differentiates paratyphoid fevers is that on the whole these are less severe, and accompanied by a lower mortality than typhoid fever.

The diagnosis of typhoid fever, though easy in some cases, may be very difficult in others. The symptoms may not be sufficiently prominent, especially at the onset. There may be an absence or alteration of some cardinal signs or a predominance of others which are of secondary importance in typical typhoid fever.

At the onset one may think of influenza or the eruptive fevers in children, especially measles.

Influenza generally has a sudden onset. The prodromal period, when present, is shorter than that of typhoid fever, even with a sudden onset. The temperature often rises suddenly to 104° and even 105·8° F., but does not keep long at this level. Sometimes it drops suddenly after two or three days and does not rise again; sometimes, after a remarkably sudden fall lasting for twelve to twenty-four hours, it rises as high again as before the fall, thus forming a depression like an upturned bell (the influenzal **V** of J. Teissier), and sometimes it descends by lysis.

According to Jaccoud, one may find insomnia,

epistaxis, delirium and ochre-coloured diarrhœa in the intestinal forms, and even hæmorrhage from the intestine (?).

The patient may present the typhoid aspect, an increase in size of the spleen, scarlatiniform and morbilliform rashes and papular eruptions (Van Swieten, Comby, Perrenot), sore throat, with redness of the pharynx and swelling of the tonsils.

But the diagnosis can be made by the oculo-nasal catarrh, arthralgia, neuralgic character of the headache, which is frequently supraorbital, frequent perspiration, and, lastly, the course of the temperature and absence of lenticular rose spots.

The history of an epidemic will be a help. One must, however, bear in mind a possible association of typhoid fever and influenza (Hérard, Moissenet, Potain).

Eruptive fevers, such as measles, smallpox or scarlatina, have a special symptomatology in the prodromal period which will, as a rule, allow them to be excluded.

In every case all doubt will be removed by the special form of the eruption when associated with a history of contagion and an epidemic.

There are numerous diseases which borrow from typhoid fever its two chief signs in the fully developed stage (viz. fever and the typhoid state), and which may cause errors in diagnosis.

Few medical men in France have seen *typhus fever*, which is characterised by its sudden onset, a temperature of 104° or 104·8° F. on the first day, with a pulse between 100 and 120, constipation with an absence of intestinal symptoms, frequent and profuse epistaxis, vaso-dilatation of the conjunctivæ (an important symptom), nasal mucosa, and upper respiratory tract, and almost constant vomiting (Bué).

The eruption of typhus appears early, being constituted by red or pink spots, which are papular and slightly elevated, disappearing at first on pressure, and appearing first on the abdomen and then invading the whole body, except the face.

After one or two days the eruption becomes darker, and the red spots become transformed into *petechiæ*, which no longer disappear on pressure.

The delirium is very violent, with a tendency to suicide, and at the end of two or three days the patient falls into a state of extreme torpor, with a congested face. In favourable cases the termination is sudden. Typhoid fever is distinguished from typhus by its slower onset, the later appearance of its eruption, which is never petechial, by the presence of intestinal symptoms, and usually by the less degree of the typhoid state.[1] If one also takes into account the highly contagious and dangerous character of typhus, it will not be confounded with typhoid fever. A blood-culture will often aid in the diagnosis.

In the first rank of febrile infections of a continuous type which may simulate typhoid fever are to be placed two forms of acute tuberculosis: miliary tuberculosis and the *typho-tuberculosis of Landouzy*.

Acute miliary tuberculosis has a less regular temperature curve, frequently showing great oscillations and sometimes assuming the inverse type.

The pulse, which is more rapid than in typhoid fever, is rarely dicrotic and closely follows the temperature. The pulmonary signs are more marked and accompanied with intense dyspnœa.

Photophobia is frequent, the digestive symptoms are less intense, the tongue remains moist for a long time, being only slightly coated, the appetite fairly often is only diminished. The abdomen is flattened or scaphoid, without any pain or gurgling, rose spots are quite the exception, the typhoid state is much less pronounced, and there may be muscular and cutaneous hyperæsthesia.

[1] In war time, however, the gravity of the general signs of typhoid fever and the symptoms of torpor are sometimes so marked that the mistake has been made. The purpuric or hæmorrhagic character of the rose spots has also suggested typhus. But in such cases cultivation of the blood during life, or of the bile after death, has yielded the typhoid bacillus.

On the other hand, the spleen may be enlarged as in typhoid fever.

The typho-tuberculosis of Landouzy bears a great resemblance to typhoid fever, especially at the onset. Its onset is slow and progressive, with pains in the limbs, headache, epistaxis, slight shivering, abdominal disturbance, occasional vomiting, constipation or diarrhœa.

There are no lenticular rose spots, however, nor ochre-coloured diarrhœa. The temperature shows great oscillations, which may be as much as 2·6 or 3·6° F. The dyspnœa is very intense in contrast with the lesions detected. A pleural localisation may occur towards the third or fourth week. It must not be forgotten that typhoid fever may present the same lesions or wake into activity latent tuberculous lesions of the pleura.

The infections due to Thiercelin's *enterococcus* are usually mild, but may be abnormally protracted and give rise to irregular pyrexia with headache, thickly-coated tongue, vomiting, abdominal meteorism, and profuse diarrhœa. The spleen is somewhat enlarged. There are no rose spots. But typhoid fever may be simulated by the duration of severe attacks of entero-coccal infection, which may last two or three weeks or more. Diagnosis can be made by a blood-culture.

Mediterranean fever (melitococcus infection, Malta fever) starts like typhoid fever, and may frequently be mistaken for it at the onset.

The patient complains of headache, pain in the limbs, and loss of appetite; the tongue is coated, vomiting is not uncommon.

Furthermore, a progressive rise of temperature with a morning remission is observed. Pains in the joints are frequent. Attention should be aroused by the obstinate constipation, and sweating at each morning remission. The patient is pale and asthenic, and the spleen is slightly enlarged. Defervescence occurs by lysis, and apyrexia becomes complete in about three weeks, but is not permanent. A fresh rise of tempera-

ture, similar to the first, occurs some days later, then a third, and so on.

The disease generally ends by recovery, but may last two or three months, one or two years, or more. It is characterised by the temperature curve, which has given it the name of "Undulant fever," or "fever with relapses." It is obvious that a diagnosis based exclusively on this temperature is too late to be of use.

Blood-culture and Wright's serum test (performed with an emulsion of a pure culture of the *micrococcus melitensis* on agar) may be carried out early in the disease, the specific agglutinins appearing on the fifth day.

In hot countries, especially along the Mediterranean coast (Salonica, Greece, Turkey, Syria, Asia Minor, etc.), *malaria* often assumes a *continuous* type, with digestive disorders, dry and coated tongue, bilious vomiting, diarrhœa, swollen and tender liver, large spleen, headache, insomnia, etc. The febrile state is prolonged in patients who are not treated with quinine. These forms of so-called tropical malaria, which are sometimes very severe, are often confounded with typhoid and paratyphoid fevers. Their onset is usually sudden. The temperature is irregular (except in the remittent type). There are no rose spots. The blood culture for typhoid and paratyphoid bacilli is negative. Examination of the blood shows an occasionally considerable proportion of schizontes and gametes. Lastly an energetic quinine treatment (2 grammes of hydrochlorate of quinine daily or two subcutaneous injections) causes a rapid disappearance of the symptoms.

It should not be forgotten that typhoid or paratyphoid fevers may be associated with malaria (typho-malarial fever).

Acute articular rheumatism may sometimes simulate typhoid fever and begin with sore throat, shivering, pains all over the body, epistaxis and fever. Sometimes it assumes an ataxic and adynamic form like severe typhoid fever. But the patient sweats profusely,

and the localisation of the pain in the joints soon forms a guide to the diagnosis.

Icterus gravis begins with symptoms which simulate the onset of typhoid fever. After a few days of malaise, pains in the limbs, headache, myalgia, and fever, or after some vague gastro-intestinal disturbance, jaundice develops, which may be insignificant or pronounced. But soon various hæmorrhages are observed, such as epistaxis, hæmaturia, hæmatemesis, intestinal hæmorrhage, purpura, ecchymosis, etc., accompanied or followed by more or less intense nervous symptoms, such as hiccough, vomiting, delirium, convulsions and dyspnœa. Death in coma may occur very rapidly, with ataxo-adynamic symptoms and a high or subnormal temperature.

It must not be forgotten that secondary icterus gravis may appear in typhoid and paratyphoid fevers, and that in many cases icterus merely indicates a primary localisation of the typhoid or paratyphoid bacillus in the bile passages.

A *typhoid form of infective endocarditis* has been described, characterised by shivering from the day of onset and high temperature, with pulmonary congestion, abdominal distension, diarrhœa, enlargement of the spleen, and typhoid state. The diagnosis may be difficult. The cardiac lesions, however, indicated by the presence of murmurs at the orifices, the absence of lenticular rose spots, the course of the symptoms when nothing is to be found on auscultation, and the development of emboli in various situations accompanied by shivering indicating sepsis, will be a help in diagnosis, though this can be rendered certain only by a blood-culture.

Apart from the insidious form of pneumonia which appears at different periods of typhoid fever, and is irregular in its course and symptoms (Dieulafoy), a *lobar pneumonia*, on rare occasions, may mark the onset of typhoid fever. "In the course of the first week the symptoms peculiar to pneumonia subside, and are followed by the signs of typhoid fever—swelling of the

spleen, rose spots and iliac pain " (Potain). In such cases the evolution of the disease will be a guide to a diagnosis.

Acute nephritis may have a violent onset, with pains in the loins, shivering, high temperature and scanty and dark-coloured urine.

One may think of typhoid fever, but the rapid and early appearance of the œdema, the puffiness and pallor of the face, the intensity of the albuminuria, and the frequent hæmaturia, will attract attention to the renal system.

Pyœmia, septicœmia and *puerperal fever* sometimes present a collection of symptoms which may suggest typhoid fever, such as prolonged pyrexia, distension of the abdomen, diarrhœa and typhoid state. The absence of lenticular rose spots, the oscillations of the temperature, shivering and profuse sweats which accompany these conditions, as well as the characteristic local symptoms and the circumstances in which they develop, will usually be enough to distinguish them.

Malignant hypertoxic syphilis may sometimes simulate typhoid fever so closely that Fournier has described it by the name of *syphilitic typhosis*. Numerous cases have been published (Dieulafoy, Morin, Courtaux, Vialaneix, Letulle, etc.). The typhoid phenomena usually appear during the eruption of the secondary stage. The temperature reaches 104°, the rise being accompanied by epistaxis, vomiting, headache, giddiness, prostration and adynamia. Dyspnœa and tachycardia are not uncommon. Death from collapse may occur. The diagnosis will be established by the history of syphilitic infection and a knowledge of the actual lesion, the absence of abdominal symptoms or enlargement of the spleen, the appearance of the syphilitic roseola, negative blood-culture, and Wassermann's reaction.

The practitioner is often uncertain, especially in the case of a child, as to whether his patient is suffering from *tuberculous meningitis* or typhoid fever. He is

all the more so, inasmuch as " pyrexia with remissions, headache, delirium, vomiting, cerebral maculæ, and even partial palsy, inequality of pupils, rolling the head from side to side, and the hydrocephalic cry may occur in both diseases " (Murchison).

In meningitis vomiting is more frequent, the tongue is not dry, there is no ochre-coloured diarrhœa to cause a special stain on the linen, the abdomen is contracted and not painful, the spleen is not enlarged, there is no intestinal hæmorrhage or epistaxis, the headache is more intense than in typhoid fever, and is accompanied by photophobia and tenderness of the eyeballs, and sometimes by strabismus. The trismus, cutaneous and muscular hyperæsthesia, irritability, gun-hammer position and presence of Kernig's sign will also be in favour of meningitis. Lumbar puncture and a blood-culture will decide the question.

It must not be forgotten that in the course of typhoid fever there may be actual meningitis and " meningeal states " due to the typhoid bacillus, and that the existence of enteric fever does not exclude the possibility of a concomitant meningitis of tuberculous meningococcal or other nature.

Among the other numerous diseases which may be confounded with typhoid fever, we may mention the *typhoid form of lumbricosis* (Chauffard), *acute osteomyelitis*, *appendicitis at the onset*, *cholera during the stage of reaction*, *acute glanders*, *acute trichinosis*, etc., etc.

In conclusion, we will give an account of two methods employed in the diagnosis of typhoid fever: Chantemesse's ophthalmo-reaction and Vincent's spleno-reaction.

Chantemesse's ophthalmo-reaction.—Chantemesse has proposed Calmette's method for the diagnosis of tuberculosis. A drop of water containing $\frac{1}{50}$ milligramme of a powder obtained by precipitation (with absolute alcohol) of a strong solution of soluble typhoid toxin is dropped into the patient's eye. The temperature and general condition are not affected. In persons not suffering from typhoid fever a little redness and

lacrymation are observed in two or three hours. In typhoid patients the reaction is more pronounced (redness, lacrymation and production of a sero-fibrinous exudate). The reaction reaches its maximum in from six to twelve hours, and continues till the next day. Experiments have been made with a cuti-reaction, but the results are very uncertain.

Vincent's spleno-diagnosis.—Enlargement of the spleen being the rule in typhoid fever, it occurred to Vincent that the inoculation of additional antigen (2 c.c. of a concentrated autolysat of living typhoid bacilli sterilised by ether) might result in causing a splenic reaction which would be useful for diagnostic purposes.

In healthy persons, or those suffering from other diseases than typhoid fever, no splenic reaction is observed; but in patients with genuine typhoid fever one finds, on careful percussion, an increase in size of the spleen by one or two centimetres in both diameters. This spleno-reaction is found, as a rule, ten to eighteen hours after the injection, very rarely later.

It has been observed in 94 per cent., and in 35 per cent. it is accompanied by enlargement of the liver.

Inoculation of an autolysat of paratyphoid B bacilli in patients suffering from paratyphoid fever B has produced a similar spleno-reaction.

The spleen responds to a specific irritation by an equally specific enlargement.

After injection of paratyphoid B autolysat in the course of paratyphoid fever B, increase in the size of the spleen generally appears less marked than after the injection of the typhoid autolysat in typhoid fever, though it is often very definite. Sometimes this increase in size is more marked after the second or third injection than after the first (Rathery), a circumstance due to the dose of antigen injected.

The value of the spleno-reaction is that it enables us to make a diagnosis earlier than a blood-culture, and, what is still more important, before the appearance of clinical symptoms.

II. Diagnosis by Laboratory Methods

The differential diagnosis of typhoid and paratyphoid fevers being, as we have seen, a difficult matter, it is necessary to resort to laboratory examination as soon as the existence of one of these diseases is suspected. The discovery, isolation and identification of the causal agent are usually possible if the investigation is made under favourable conditions.

Our study will be divided into two parts, the first dealing with the methods of investigating the bacillus, and the second with the humoral reactions of the organism.

Investigation of the bacillus. The typhoid bacillus is known to exist in the *blood* throughout the duration of the infection. It persists through the height of the disease, and usually disappears at the end of the third week, but it may be found in the blood even later.

After being carried into the organism by the circulation it may be localised and multiply in any organ, especially the spleen, liver, bile passages, bone marrow and mesenteric glands.

It is also found in the lenticular rose spots. It is present in the intestine several days before the appearance of the first symptoms. The number of bacilli in the fæces increases until the end of the first week, and gradually disappears at the end of the fourth.

The typhoid bacillus fairly frequently passes into the urine (Bouchard). Vincent found it in the urine in about a fifth of his typhoid cases. It sometimes persists in the fæces and urine after recovery, when the bacilli are growing in the gall bladder and bladder. According to Besson, the typhoid bacillus is found in albuminous urine exclusively. It hardly ever appears in the urine before the tenth day, and as a rule not before the fifteenth. In the urine and fæces the elimination takes place intermittently.

The typhoid bacillus has been found in the pharyngeal ulcers and in the deposit on the teeth.

Lastly, it has been isolated as the causal organism

of a large number of complications, such as tonsillitis, rhinopharyngitis, laryngo-typhoid, pleurisy, pneumonia, adenitis, abscesses, osteitis, etc., etc.

As will be seen from this list, the infective agent may be found in every possible situation. Where should the investigation be made to obtain an invariably positive result?

The bacillus can be most frequently isolated by puncture of the spleen, but this method is dangerous, as the organ can easily be torn if the patient makes a sudden movement.

Search for the bacillus in the stools is a delicate process, in which much depends upon good luck. The isolation of typhoid or paratyphoid bacilli from the stools is often difficult, owing to the large numbers of bacteria living in the intestine. This investigation, however, presents a great prophylactic and epidemiological interest, being usually employed for detecting germ-carriers and determining how long a convalescent may remain contagious. It is therefore advisable to describe the usual methods.

Plugs of mucus are sought for in the stools, washed once or twice in normal saline solution, and then planted on an appropriate medium. According to the method advocated by Sacquépée and Bellot, the large intestine is washed out twice with a litre of boiled water, it is then washed out a third time and the last part of the evacuated fluid is kept for analysis.

P. Carnot and Weill-Hallé recommend the following method: Fill one of the branches of a U tube of 5–6 millimetres in diameter with a layer of fine sand up to 10 centimetres. Pour some broth coloured with neutral red into the other branch of the tube until the broth is at the same level in the two branches a little above the sand. Then add to the broth in the second branch some drops of the almost clear fluid obtained from a second intestinal wash-out following a preliminary evacuant enema. Examine after eighteen hours' incubation. The duration of the stay in the incubator is in proportion to the height of the layer

of sand and the motility of the bacilli. The higher the level of the layer of sand, the more accurate will be the result of the examination of the micro-organisms.

The stay in the incubator may be reduced to six hours when the height of the sand is about three centimetres. The broth above the level of sand has either retained its colour but become turbid, or it has changed to a fluorescent yellow. In the first case the typhoid bacillus only, which is usually by far the most motile organism, has been able to pass through the sand and grow; in the second case the paratyphoid bacilli A and B, or the bacillus coli, have done so too. A microscopical examination is made, before and after staining by Gram's method. If bacilli are found which are not stained by Gram, they are isolated on Endo's agar or Drigalski-Conradi's medium in Petri's capsules. All the colonies stained red are disregarded. Only those colonies which are unstained, or stained a very faint pink or blue, are to be examined. Each of these will have to be identified by growth on special media, and by the examination of their agglutinability.

It is possible to isolate the bacilli from the lenticular rose spots. Chauffard and J. Troisier, by injecting subcutaneously into typhoid patients $\frac{1}{5000}$th of the dose of toxin fatal to a guinea-pig weighing 250 grammes, succeeded in reproducing a typical lenticular rose spot which is generally identical with the patient's spontaneous rose spots. This artificial rose spot may fail to appear in some typhoid patients: its duration, when it does appear, does not exceed twenty-four to forty-eight hours. In the typhoid patient it indicates the presence of an intradermic colony of micro-organisms. After washing the skin with soap, and then with alcohol, prick the spot with a needle, a small bistouri or a vaccinostyle. Aspirate with a sterile pipette the drop of blood which wells out through the little opening, and grow it in a tube of bile broth and in the water of condensation obtained from agar tubes.

By inclining these tubes the surface of the agar is moistened with the water of condensation, and the

micro-organisms are thus distributed all over the surface of the medium.

It has been said that typhoid *bacteriuria* is a late event. Its investigation is only of interest for prophylaxis and epidemiology. The clot obtained aseptically by centrifugalisation of the urine should be planted on Endo's medium.

The *pus* obtained from various sources and the *sputum* should also be grown (1) in bile broth, (2) in agar poured into Petri's capsules. The organic media in which the typhoid and paratyphoid bacilli are to be sought for during life are the blood and bile, and after death the heart blood and spleen pulp.

Culture from the bile.—Bur, Hautefeuille and Sevestre have found typhoid and paratyphoid bacilli by taking cultures from the bilious vomit which is often seen in typhoid and paratyphoid fevers. Boldyrev and Volhard have shown that the introduction of a certain quantity of oil into the stomach is followed by a reflux of bile mixed with pancreatic juice. Weber (in 1909, in two cases) and Kiralyfi (in 1912, in sixty-nine examinations of thirty cases) availed themselves of this property for the purpose of removing bile during life, cultivating it and obtaining postive results. After having washed out the stomach of a fasting patient with sterilised distilled water, 250–300 c.c. of sterilised olive oil are introduced by the same funnel. In half an hour's time the oil is withdrawn. The patient must be told not to swallow his saliva, as it will increase the number of micro-organisms in the stomach contents.

After the fluid has been collected in a sterilised recipient, it separates at once into two layers, the upper formed by the oil and the lower containing the bile. Carnot and Weill-Hallé administer only 50–150 grammes of olive oil, which they remove by gastric intubation three hours later.

In the exceptional cases where gastric mucus only is withdrawn, it should be cultivated, for the typhoid bacillus may be found in it fairly often, although less constantly than in the bile.

Carnot and Weill-Hallé also perform direct intubation of the duodenum by making the patient swallow a rubber tube of about three millimetres in diameter and one metre long, terminated by a little glass nozzle, open at the two ends, which has been carefully sterilised and is protected by the rubber tube up to its terminal orifice. The patient swallows eighty centimetres of the tube, which is left in position for three hours, sometimes four, by which time the nozzle has passed through the pylorus and penetrated into the duodenum. Aspiration is then made with a syringe fitted to the outer end of the rubber tube. If the nozzle is in the right position, almost pure bile is withdrawn.

The writers themselves admit that this technique is not always easy to carry out "in some typhoid patients in a state of prostration, who are incapable of executing intelligently the measures required."

These two processes, however, give almost the same results.

Carnot and Weill-Hallé regard cultivation of the bile as a measure possessing great prophylactic importance. In most cases it yields results later than blood-culture. It cannot be carried out before the end of the first week, but it enables us to trace a carrier long after the disease has come to an end. Thus the writers found the typhoid bacillus in the bile after the sixth month.

Blood-culture.—Very numerous methods have been employed. It would be tedious and unnecessary to describe them all. As the blood serum possesses strongly bactericidal properties, some recommend that a fairly large quantity of blood should be grown on a very large quantity of a fluid-culture medium. The blood is taken by aseptic puncture of a vein at the fold of the elbow. Ten to twenty c.c. are collected and put in a litre of beef broth, or, more economically, following H. Lemierre's example, in ordinary peptone solution prepared as follows—

Peptone	20	grammes
Sodium chloride	5	„
Water	1000	„

This process, which has been copied from Castellani and Busquet, has been employed for several years by J. Sabrazès, who prefers it to others as being the most simple, practical and certain method. Lafforgue separates the corpuscles from the plasma after adding to the blood a 2 per cent. solution of citrate of soda (1 drop per c.c. of blood), centrifugalises it and pours the clot into broth-tubes.

In the course of this war bacteriologists have endeavoured to discover the most favourable culture medium, and one which does not require elaborate apparatus.

Bile has been chiefly in favour, either in a pure state after sterilisation, or associated with beef broth, Liebig's extract, or peptone solution. The media with a bile base possess the great advantage of avoiding the coagulation of blood and of forming an excellent soil for the cultivation of typhoid and paratyphoid bacilli.

Filtered bile, diluted to a third or half of its volume by broth or peptone solution, appears best.

P. Carnot and Weill-Hallé have also employed U tubes with a sand filter two centimetres high for blood-culture. Into one of the branches of the tube they put the mixture of sterilised ox bile (five c.c.) and the patient's blood (twenty to thirty drops), and into the other a sterile broth. The motile bacilli growing in the bile pass through the layer of sand and multiply in the broth, where they can be much more easily examined on the following day.

Muratet, in his field laboratory, has availed himself of this process, which has been of great service to him, with the following slight modifications.

The tubes are larger than those of Carnot and Weill-Hallé. Two to three c.c. of blood are grown in one of the branches of the U tube containing five c.c. of ox bile and five c.c. of peptone solution. Into the other branch is poured broth coloured with neutral red (Savage's medium). When the blood-culture is positive, Savage's broth may become turbid without losing its red colour, or it assumes a fluorescent yellow colour.

P. Carnot and Weill-Hallé describe a still simpler process, which consists in making a culture of pure bile and then introducing a layer of broth above the bile-blood medium, taking care to avoid a mixture. The culture may be made in an ordinary test tube which presents a certain advantage, for the manufacture of U tubes is not always easy in the army on active service, and these tubes often break in the course of sterilisation or manipulation.

When fresh ox bile is not available, dried bile, or the "ox gall," to be obtained from a chemist's, may be dissolved in peptone solution. This method gives good results, and one can always have a small store of bile extract in the laboratory.

The substitution of bile salts for bile does not constitute a more favourable medium (Sabrazès).

Whatever the method employed, one proceeds as follows with the examination of the cultures and the identification of the organisms.

The first microscopical examination may be made with a slide and coverslip or with a hanging drop-culture, without staining, to see if the bacilli, whether motile or non-motile, have grown. In positive cases, if the bacilli are motile and are not stained by Gram, we may be dealing with one of the micro-organisms of the colityphoid group.

As regards these cultural reactions, generally speaking the paratyphoid A bacillus resembles the typhoid bacillus, and the paratyphoid B bacillus the bacillus coli. Paratyphoid bacilli are motile, do not stain by Gram, possess 8–10 flagella and are facultative anærobes. They cause fermentation in glucose, mannite, dulcite, lævulose, maltose and galactose, but not in lactose, raffinose or cane sugar. They differ, therefore, from the typhoid bacillus, which does not ferment any sugar. They do not coagulate milk or produce indol, which differentiates them from the bacillus coli, which ferments all sugars. One should bear in mind the existence of infections due to the *B. fæcalis alcaligenes* and the properties of this micro-organism, which, though very like the

TABLE OF THE PRINCIPAL DIFFERENCES BETWEEN THE TYPHOID BACILLUS, PARATYPHOID A BACILLUS, PARATYPHOID B BACILLUS AND BACILLUS COLI.

Diagnostic method	Typhoid bacillus	Paratyphoid A bacillus	Paratyphoid B bacillus	Bacillus coli
Odour.	No special odour.	No special odour as a rule, but sometimes a slight odour.	Disagreeable or fæcaloid odour.	Fæcaloid or fishy odour.
Motility.	Usually very motile.	Motile.	Motile.	Very variable. Usually motile, but less so than typhoid bacillus. May be non-motile.
Growth on potatoes.	Damp, faint, glistening track, then brown tint.	Damp, faint, glistening track.	Thick, shining brownish growth, sometimes scanty.	Prominent yellowish or brownish film.
Growth on artichokes.	No green coloration.	Green coloration absent or very late.	Green coloration in 2 or 3 days.	Green coloration rapid.
Growth in milk.	No change.	No change.	Becomes clear and turns brown after eighth day.	Clotting usually in 24–48 hours.
Growth in litmus milk or whey.	Slight acidity (pink tint).	Slight acidity (pink tint).	Slight acidity (pink tint) in first few hours, then alkalinisation (blue tint) from 3rd–7th day, sometimes very late (18th–20th) day).	Clotting of milk, red coloration in 24 hours.

Growth on lactose, raffinose or saccharose media.	Acid. No gas.	Acid. No gas.	Acid. No gas.	Acid. Production of gas.
Growth on glucose, lævulose, maltose, galactose, mannite and dulcite media.	Acid. No gas.	Acid. Production of gas.	Acid. Production of gas.	Acid. Production of gas.
Growth on glucose-neutral-red-agar.	No change.	Decoloration, fluorescence, fragmentation of the medium.	Decoloration, fluorescence, fragmentation of the medium.	Decoloration, fluorescence, fragmentation of the medium.
Growth on decolorised fuchsia-agar (Endo).	Colourless colonies.	Colourless colonies.	Colourless colonies.	Red colonies.
Growth on lactose-litmus - crystal - violet - agar (Drigalski-Conradi).	Blue transparent colonies.	Blue transparent colonies.	Blue transparent colonies.	Red opaque colonies.
Growth on subacetate of lead medium.	Blackening.	No blackening.	Blackening.	No blackening. Some exceptions.
Formation of indol.	No indol.	No indol.	No indol, or only traces.	Production of indol.

typhoid bacillus, nevertheless turns litmus milk strongly alkaline.

The identification of the organisms isolated must be completed by *a study of their agglutinability* by means of specific experimental serums. The serums employed for this purpose must be of moderate strength, 1 per 1000 to 1 per 10,000. They have sometimes a marked agglutinating property for other species (coagglutination). The largest possible number of typhoid bacilli are agglutinated in the same degree by the same experimental serum.

Some bacilli, however, which have been recently isolated from the blood, fæces or water, are not agglutinable, although they possess all the characters of the typhoid bacillus. Before regarding them as genuine typhoid bacilli, they must undergo several passages through broth. By this process the genuine typhoid bacillus progressively acquires a considerable agglutinating power.

It seems that there is some parallelism between the lack of agglutinative power and the absence of motility (C. Nicolle and Trénel). The experimental serums are specific for the typhoid and paratyphoid bacilli. They agglutinate all the strains in almost the same dilution. Exception must be made for the paratyphoid B bacilli, of which the different strains are agglutinated in very unequal dilutions.

As the experimental serums contain amboceptors, the reaction of fixation of the complement can be applied for the diagnosis.

However, if this amboceptor is specific for the typhoid bacillus, this is not the case with the paratyphoid bacilli A and B.

Experimental serums deviate the complement in the presence of the paratyphoid bacilli with which they have been obtained, but the experimental serum obtained with the paratyphoid A bacillus contains an amboceptor, which acts equally on the typhoid bacillus and the paratyphoid B bacillus.

In like manner, the experimental serum obtained

with the paratyphoid B bacillus contains an amboceptor which also acts on the typhoid bacillus (Rieux and Sacquépée).

We cannot close this chapter, which is necessarily very incomplete, without reminding our readers that in diseases resembling typhoid fever pathogenic micro-organisms, differing from the typhoid and paratyphoid bacilli by one or more characters reputed to be specific, have been isolated during life by means of blood-culture.

They may be described as "intermediate bacilli" to indicate that they belong to a group which possesses some of the characters of the typhoid and paratyphoid bacilli, without any suggestion that they represent a stage of passage from one micro-organism to the other. Cases of this kind have been published by Moutier, Faroy, Lecount and Kirby, Lafforgue, etc. A certain number of cases has also been published in which *the clinical symptoms were like those of typhoid or paratyphoid fever*, but in which *B. fæcalis alkaligenes* was isolated by blood-culture.

This micro-organism undoubtedly possesses pathogenic properties for man, giving rise to infections which are sometimes mild and sometimes remarkably severe, especially in Morocco. The symptoms, and even the character of the autopsy lesions, may resemble those of typhoid fever. The study of this micro-organism should be carefully pursued.

Lastly, there has been found in the patients' blood, in addition to the typhoid or paratyphoid bacilli, a certain number of pathogenic micro-organisms, such as the micrococcus melitensis (Bassères, Rauzier and Roger, Laggrifoul, Arnal and Roger), proteus vulgaris (Vincent), staphylococcus, streptococcus (Vincent), bacillus pyocyaneus (Vincent), hæmamœba malariæ (Kelsch and Kiener, Vincent), etc., etc.

Sometimes one of the paratyphoid bacilli, especially B, may be found at the same time as the typhoid bacillus (C. Gautier and R. J. Weissenbach).

The presence of these micro-organisms gives a special character to the typhoid infection, completely modifies

its characters, and sometimes considerably increases its gravity.

III. Study of the more or less Specific Humoral Reactions caused in the Organism by Typhoid Infections

Widal's serum test.—In a previous chapter we indicated the principle of this test. We must now discuss in detail some special points.

Normally human serum agglutinates the typhoid bacillus at 1 in 10–1 in 20, and the paratyphoid bacilli at 1 in 50, even at 1 in 150 (Sacquépée, Chevrel, Béco). In the course of typhoid or paratyphoid infections human serum acquires agglutinating properties. But these properties may be absent. They generally appear towards the end of the first week, and, on the average, acquire their maximum from the twelfth to the twentieth day. Besides the blood serum, nurse's milk (Achard and Bensaude), urine, tears, pleural fluid and cerebrospinal fluid (Brandéis and Mongour) may be endowed with agglutinating power. The mother can transmit it to the fœtus.

This agglutinating power is not absolutely specific. Side by side with agglutinins there exist group coagglutinins.

Thus the serum of patients suffering from typhoid fever may agglutinate paratyphoid A and B bacilli *as much as*, and *even more than*, the typhoid bacillus (Sacquépée). Likewise, the serum of patients suffering from paratyphoid A infection agglutinates paratyphoid A bacilli in low dilution (1 in 100 or 1 in 200), but it may agglutinate the typhoid bacillus and paratyphoid B bacillus in the same dilution. The serum of patients with paratyphoid B infection can agglutinate very energetically the patient's own bacillus (even up to 1 in 40,000), but much less other bacilli of the B type (1 in 100–1 in 1000). It is much less active, as regards the typhoid bacillus and paratyphoid A baccillus. An attempt has been made to get rid of these coagglutinins

by Castellani's process. But this test, which is accurate in the case of experimental serums, is much less reliable in the case of human serums, and its clinical value is doubtful (Rieux and Sacquépée.) To make use of the reaction it has been necessary to standardise, so to speak, the agglutinating power of the serum for the typhoid bacillus and paratyphoid bacilli A and B. Dilutions had to be pushed to extreme limits, and only strong dilutions were taken into account. Paradoxical agglutinations, nevertheless, will still be met with. Some writers, however, state that one can make a diagnosis of typhoid infection if human serum agglutinates the typhoid bacillus at a minimum dilution of 1 in 150–1 in 200, and in a much lesser degree the paratyphoid bacilli (M. Labbé, Cade and Vaucher). According to Salomon, in the presence of a negative blood-culture recourse should be made to the serum test, even in the inoculated. One may " regard as of value agglutinations for paratyphoid A and B occurring at a minimum dilution of 1 in 200, but importance should only be attached to agglutinations of the typhoid bacillus when they are definite and intense in dilutions of, or exceeding, 1 in 500."

In cases where a serum agglutinates a paratyphoid bacillus more than a typhoid bacillus, " nothing allows us at present to conclude that we are in presence of a paratyphoid infection " (Sacquépée and Chevrel). According to Rist, the specificity of the serum reaction is still less certain. " The serum reaction is of no value as a guide as to whether the typhoid bacillus or paratyphoid A or paratyphoid B bacillus is the cause of the disease. Blood-culture alone enables us to differentiate them. A positive serum agglutination in the non-inoculated fully authorises us to say ' this is a typhoid fever;' it is unable to determine which of the three micro-organisms should be incriminated."

If the diagnostic value of the serum reaction is only relative in the non-vaccinated, what is to be said of it in those who have been vaccinated ?

It is known that antityphoid vaccination causes the

appearance of powerful agglutinins in the blood serum. This agglutinating power, which may, exceptionally, be as high as 1 in 5000 or 1 in 10,000, falls fairly rapidly to 1 in 50 or 1 in 10, and even completely disappears three or four months after the last injection of vaccine. This agglutinating power may be wakened into fresh activity by any kind of disease of a non-typhoid nature (pneumonia, appendicitis, dysentery, rheumatism, ordinary sore throat, simple diarrhœa, etc.), and also by paratyphoid fever, when it rises to a considerable figure: 1 in 400 six months after antityphoid vaccination, 1 in 200 twenty-five months after vaccination with five injections, etc. (Rist, Coyon).

However that may be, at the present time millions of men have undergone typhoid and antityphoid vaccination. Owing to this fact their serum contains active or latent agglutinins for the typhoid bacillus and the paratyphoid A and B bacilli.

The results of the serum test, if performed in such cases, would be of no value for the diagnosis of typhoid and paratyphoid fevers. This is the view of Léon Bernard and Paraf: "Its results, which were already irregular and open to suspicion in subjects who had not been inoculated, are absolutely useless in those who have been; the application of this method for that purpose can only give rise to error."

This is also the opinion of Rist, who says, "In those who have been vaccinated, even with a single injection, the agglutination test ought not to be regarded as a diagnostic method. Not only does it fail to distinguish typhoid fever from paratyphoid, but it cannot even serve to discriminate an infection of the typhoid group from any febrile disease whatever. This diagnosis can only be established by a blood-culture or clinical examination."

Reservations must also be made as to the value of the clinical factor.

This is likewise the opinion of all those who have been working in army laboratories or ambulances. In the light of established facts they have had to give up their

confidence in the agglutinating serum reaction and follow the rule which H. Vincent laid down some time ago. " The blood of every inoculated person agglutinates the typhoid bacillus more or less. This agglutinating power may be aroused or exaggerated by any kind of acute infection occurring in the vaccinated. No value, therefore, should be attributed to the agglutination test as regards the diagnosis of any subsequent illness. Blood-culture alone gives precise information."

The reaction of fixation of the complement.—The blood serum of patients suffering from typhoid or paratyphoid infections contains amboceptors, which Widal and Le Sourd have detected by the ordinary method of fixation of the complement (Bordet and Gengou). These amboceptors, however, are not strictly specific (Rieux and Sacquépée). In addition to specific amboceptors there are group amboceptors, as in the case of agglutination.

It is the same with human serum as with experimental serum, and with amboceptors as with agglutinins : a real diagnostic certainty is not always obtained by investigating them.

Determination of the opsonic index.—Wright has shown that special substances are present in normal and pathological blood serum, which he has called opsonins (opsono = I prepare food for), and which are indispensable for phagocytosis.

In pathological serums the amboceptors not only sensitise and bacteriolyse the pathogenic micro-organism, but also favour the phagocytosis. The value of this power is determined fairly easily in practice, and opsonic index is the name given to the relation of the opsonic power of a pathological serum to the opsonic power of a normal serum, their power being calculated for the same bacterial species.

Milhit has shown that an opsonic index for the typhoid bacillus above 1·70 in a suspected subject is an element in favour of typhoid infection if he has not already had typhoid fever.

Rathery has recently studied the opsonic index of typhoid and paratyphoid cases which have been treated by Vincent's vaccine known as autolysat. He found that during the disease the opsonic index of these patients was fairly high. From a practical point of view Rathery thinks that it is advisable to continue vaccine treatment if a fresh injection causes a definite fall in twenty-four hours' time of the opsonic index, which rises again after the second injection.

CHAPTER V

TREATMENT OF TYPHOID FEVER AND PARA-TYPHOID FEVERS

A NUMBER of methods have been suggested for the treatment of typhoid fever. These methods may be grouped according to the special aim in view. We will study successively in separate sections—

1. The hygiene of the typhoid patient; the "little attentions" that he requires.
2. The diet.
3. The methods employed to lower the temperature.
4. Various measures, including antiseptics, tonics, diuretics, and methods for combating the infection.
5. Special treatment applicable to the principal complications of typhoid fever.

Lastly, by way of completing the methods of treatment indicated in the previous sections, and which are *symptomatic measures* applicable to all typhoid infections indiscriminately, we will describe the actual state of our knowledge of *the specific treatment of typhoid and paratyphoid fevers by serum therapy and vaccine therapy.*

The hygiene of the typhoid patient.—As soon as typhoid fever is suspected, treatment should be commenced at once, without waiting for clinical or laboratory confirmation.

The patient should be isolated as soon as possible in a large, well-ventilated room, into which the sun can penetrate. The mean temperature of the room should be about 60° F. Carpets, curtains and hangings should be removed. If possible, two beds should be placed in the room, so as to change the patient from one to

the other if necessary. A waterproof sheet should be put between the sheet and the mattress, and above the sheet the bed should be provided with a draw-sheet which can be easily removed and changed as soon as it is soiled or wetted. The patient should be clad in a shirt or vest which is completely open behind. Too much light should be avoided, as well as any noise, conversation or visitors. The typhoid patient needs absolute calm and repose.

The greatest attention must be paid to the patient's bodily cleanliness and antisepsis. For this purpose a whole series of precautions and methods are required comprised under the general description of "little attentions"—a rather inaccurate term, it may be said, for these attentions are of the greatest importance in the struggle with the disease.

Toilet of the mouth and nasal fossæ.—A dry, shrivelled tongue constitutes a real danger in typhoid fever because it prevents nourishment being taken. It may also be a cause of infection and dysphagia. The tongue should not present this appearance when the patient is well looked after and well nursed. From *the onset of the disease* the nurse should be set about cleaning the mouth, and under these circumstances it will be easy to keep it clean. If, on the contrary, she waits for several days, the tongue, inside of the cheeks, teeth and gums become covered with thick, hard and adherent crusts which will be all the more difficult to remove as the patient will be unwilling to submit to this fatiguing, disagreeable and sometimes even painful operation. So from the very beginning of the disease the teeth, gums and tongue should be cleaned gently several times a day with a soft brush.

For this purpose a mixture of equal parts of glycerine and eau de Vichy or eau de Vals should be used. The mouth should be washed out with one of these mineral waters or with a four per cent. solution of boric acid. The stringy mucus should be removed from the pharynx by moist swabs of wool mounted on the end of long forceps. When the cleaning is finished the patient

should be given some drops of lemon juice, as they cause a slight stimulus to the salivary secretion. In this way the excretory channels will be swept clean. If dark crusts are seen at the back of the mouth, the pharynx must be irrigated with boiled water from a can containing hydrogen peroxide, twice in the twenty-four hours at least. These irrigations prevent the development of grave infective complications (pharyngeal ulceration, quinsy, etc.), which are exclusively due to these septic accumulations of mucus.

Once or twice a day the patient may gargle or rinse out his mouth with water rendered antiseptic by the addition of a few drops of Javel extract.

By these different methods it will be easy to keep the mouth perfectly fresh and the tongue moist and clean.

After having raised some difficulty at first, the patient will afterwards ask for these attentions of his own accord.

A careful watch should be kept for the appearance of lingual, buccal or labial ulcerations. As soon as they appear they should be touched lightly with tincture of iodine, methylene blue, chlorate of potash or even formol (Milhit).

The nasal fossæ must also be cleaned, and the crusts removed, after they have been softened with a few drops of menthol oil (50 per cent.), or with menthol vaseline oil, or, better still, gomenol vaseline. Vernier recommends the insertion into the nostrils of a plug of ointment the size of a pea of the following composition—

Vaseline	20	grammes
Boric acid	2	„
Resorcin	0·15	„
Menthol	0·05	„

The lips should be washed with warm boracic lotion. Attention must be paid to the ears, and the patients prevented from scratching their nose, nasal fossæ, etc.

Hygiene of the skin. The frequency of boils in convalescence from typhoid fever is well known. The

origin of these secondary infections of the skin, which may sometimes assume the character of phlegmonous inflammation and grave septicæmia, is often neglect of cutaneous asepsis.

Asepsis of the skin should be carried out in the following way. Plugs of cotton-wool containing carbolised glycerine may be placed in the ears. In addition to baths, the skin should be sponged all over with cold or warm water containing thymol, antiseptic or aromatic vinegar, or eau de Cologne. All the parts which have been soiled by the urine or fæces should also be washed by sponging rather than by rubbing the skin with damp wool. After each washing the parts should be gently dried. Every folliculitis lesion should be touched gently with iodine or iodine-acetone. As soon as the formation of a little vesicle filled with pus is observed, the pus should be evacuated aseptically and the little wound painted with iodine.

One must be on the look out for infections due to streptococci, staphylococci or B. pyocyaneus, and treat them if they appear with tincture of iodine or peroxide of hydrogen.

In some cases, when the infection is generalised, recourse should be had to antiseptic baths, preferably boracic acid (200 grammes per bath), to which has been added a little eau de Javel (liquor sodæ chlorinatæ). As prolonged pressure in association with maceration may cause trophic disturbances of the skin, especially bedsores, attention must be paid to the patient's position in bed, and he must be dried carefully after sponging or baths. He should never be left too long in the same position. Several times a day he should be made to change into a different position, such as the right or left lateral decubitus, the dorsal decubitus, or a half-sitting position, by supporting him with cushions or pillows. As ulcerations in typhoid patients have a rapid course, as soon as a redness is seen, especially in the gluteal region, after making the skin aseptic it should be dusted with subnitrate of bismuth and finely-pulverised Lucas-Championnière powder,

and care should be taken that the patient should always rest on a thick layer of heavily-powdered wool.

If the subject is fat, the natal cleft down to the anus should also be powdered after washing. If a slight ulceration appears, it should be painted with tincture of iodine and then powdered, and the region should be supported on a rubber ring. If the patient is thin, a water bed should be used.

The hair should be cut at the beginning of the disease, which can easily be done in men; as this practice has certain disadvantages in the case of women, their hair should be plaited in two or three very close plaits, which should be wetted as little as possible during the baths. In convalescence the plaits should be undone for a short time every day, for five to ten minutes at most, after oiling the scalp. The head may be washed with Panama soap and shampooed with St. Louis lotion (ammonia 4 grammes, oil of turpentine 25 grammes, camphorated alcohol 125 grammes).

Good results, especially in children, may be obtained with Comby's prescriptions.

The Lotion

Castor oil	30 grammes
Alcohol 60 per cent.	100 „
Tincture of quinine, Tincture of rosemary, Tincture of Jaborandi	aa 5 „

or

The Ointment

Vaseline	30 grammes
Lanoline	10 „
Balsam of Peru	2 „
Gallic acid	1 „

To be rubbed into the scalp morning and evening.

Hygiene of the genito-urinary system.—Ulceration of the vulva is not uncommon in typhoid fever. In the case of little girls the parts should be washed carefully

every day with soap and water. In women one should order vaginal douches of a 1 in 400 permanganate solution, followed by washing the vulva with soap. In severe typhoid fever one may have to catheterise the patient. In such cases the greatest antiseptic precautions must be taken; if infection is likely to occur the bladder should be systematically washed out with 250 c.c. of a very weak hot solution of permanganate of potash.

Diet of the typhoid patient. The diet of the typhoid patient is of the utmost importance. The typhoid patient must receive nourishment, but in practice views differ as to the nature of this nourishment. Generally speaking, in France the diet prescribed is fluid or semi-fluid. It chiefly consists of milk. The patient should take a minimum of three to four litres of fluid in the twenty-four hours, two of which should consist of milk. The milk should be given only after it has been boiled for at least ten minutes. It should be kept in a cool place in closed receptacles. It may be given pure or diluted with eau de Vichy or eau de Vals, or hot, warm or cold, and with or without sugar. If the patient wishes it, there is no harm in flavouring it with small quantities of tea, coffee, rum, cognac, kirsch, orange-flower water, vanilla, essence of aniseed (one drop per cup), or in making it acid or frothy, etc. After each feed of milk it is well to wash out the mouth with eau de Vichy, ptisan, orangeade, etc. If the milk is well tolerated, the quantity may be increased to two and a half litres a day. Sometimes, although it has been boiled and had not gone sour, it may cause diarrhœa and distension. It should be given in feeds of about fifty grammes at a time, to which lime water or citrate of soda (in a dose of two grammes per litre of milk) have been added. Asses' or goats' milk may be tried. In case of absolute intolerance, recourse should be had to kefir or koumiss. Silby uses whey in amounts varying from one to three and a half litres per day, flavoured with tea or coffee. Lastly, in some cases milk will have to be given up altogether and

replaced by vegetable soup,[1] cereal decoctions,[2] or soups containing flour, and eggs and very light custards.

Besides milk, the patient may take every hour, or every half-hour, half a glassful or a glassful of such drinks as wine diluted with lemonade, weak tea or coffee, weak grog, lemonade, orangeade, fruit syrups much diluted with water, slightly alkaline mineral waters (Vichy-Célestins, Vals), and diuretic decoctions (couch-grass, cherry stalks, liquorice, etc.). The drinks may be given warm, at the room temperature, or even iced. They should not be made too sweet, as an excess of sugar may increase intestinal fermentation. Lactose, which is diuretic, may be used, in a dose of 100–200 grammes per diem, to sweeten the drinks.

The patient should drink often, but little at a time, and very slowly.

Apart from exceptions based on the general state, appearance of the tongue and the temperature, he should not be woken up for a drink, but all suitable occasions should be made use of. The best times, and those when he will be most ready for a drink, are after

[1] Vegetable soups are much used in the treatment of children's diseases. Among the numerous prescriptions, Méry's formula is to be recommended.

Potatoes	60 grammes
Carrots	45 „
Turnips	15 „
Dried peas	6 „
Dried beans	6 „
Cold water	1 litre
Salt	5 grammes

Boil for two hours; filter; make the filtrate up to a litre by adding cold boiled water. Add 5 grammes of salt.

[2]

Barley, Pearl barley, Pounded maize, Shelled beans, Shelled peas, Shelled lentils	30 grammes or a ladleful of each

Boil for three hours in a litre of water, add 5 grammes of salt and strain.

the cleaning of the mouth, and during and after the bath at the moment of reaction.

Milk and drinks are not always sufficient nourishment for typhoid patients.

Robin adds a litre of veal or chicken broth in the twenty-four hours.

It rarely happens in the course of typhoid fever of moderate intensity that one can make the patient take all the nourishment he needs. As a rule he takes much less. Sometimes, even, he refuses all nourishment. One is forced to feed him by a tube, or, which is much less desirable, carefully give him nutrient enemata containing milk and peptone and the yolk of an egg. The patient's refusal to take food is hardly ever persistent; in a few days' time he usually consents to take any kind of nourishment.

The regime which we described should be continued till the time when the temperature has definitely fallen and keeps below 98·6°. As soon as the general condition improves and the temperature falls to about 98·6°, the patient begins to have a craving for food. The doctor must make the convalescent understand that a too hasty return to substantial food exposes him to a relapse, which may be grave, and even fatal. The patient's attendants and family should be warned of all the dangers that may be caused by indulging the convalescent's immoderate appetite even in a slight degree.

As a general rule, while the temperature fluctuates between 98·6 and 99·6° he may take three litres of milk or broth. He may also be given a light, well-cooked tapioca pudding.

If the temperature keeps at about 98·6°, one may gradually try a little more substantial diet, for very often inanition in emaciated and debilitated subjects is enough to maintain a slight rise of temperature, which disappears as soon as the patient takes a little more nourishment. But in most cases one must wait till the temperature has been normal for three or four days. Then, very cautiously, keeping an eye on the tempera-

ture and the stools, one may give a little well-cooked tapioca or semolina in some meat or chicken broth, with the daily addition of the yolks of one or two eggs. If the temperature does not rise the patient may take two soups of a somewhat thicker consistency, and then *purées*. Lastly, he may be allowed a small piece of stale bread, without crust, in the soup, with a boiled egg and jam, and then successively a little fresh fish, chicken, beef or mutton, with the order to eat it slowly and masticate it well. If the fever reappears, he should return immediately to milk and broth. If the patient does not have a stool daily, his bowels should be moved by prunes, stewed fruit, or an enema of cold water.

Such is the diet which almost all French physicians have ordered their patients. Other scales of diet have been advocated.

Johnson and Watt do not give milk until convalescence. Their patients' diet is composed of soup made of barley meal, rice, oats, eggs and sugar. They use large quantities of gelatin.

This diet cannot escape criticism. In addition to its nutritive properties, milk has also diuretic properties which the most nutritious broth does not possess. Gelatin may combat and even prevent diarrhœa and hæmorrhage, but it is not nutritious, and, even by flavouring it, it is difficult to mask its disagreeable taste and make the patient take fifty grammes of it daily for several weeks.

A certain number of Russian authors (Gournitzki, Botkine, Puritz, etc.) and Vaquez, in France, with the object of preventing excessive emaciation and shortening the duration of convalescence, give substantial nourishment to their patients.

They maintain that the temperature is not increased, the risks of perforation and hæmorrhage not greater, nor relapses more frequent in consequence of their method. Although he does not, like the Russian authors, go so far as to give his typhoid patients soup, rissoles, cutlets and potatoes, Vaquez's diet is nevertheless a very generous one. Every two hours the patient

has a cup of milk, but at 8 a.m., noon and 6 p.m. a small meal may be substituted for this cup of milk. At 8 a.m., a cup of tea or coffee and milk, or a plate of farinaceous soup (raccahout, barley or rice); at noon, bread and milk with a yolk of an egg, a wineglassful of meat jelly or cold meat juice; at 6 p.m., the same meal but with some broth with an egg beaten up substituted for the bread and milk. In the night a similar little meal with milk. The principal meals are given on leaving the bath. When the temperature falls, grated raw meat, such as mutton or pork, is given. Then various soups, rice pudding and potatoes, until on the eighth day of convalescence the patient is given biscuits, boiled eggs, etc.

This method has been criticised. In any case, it is not suitable for severe attacks.

Claisse gives a small meal every four hours to his typhoid patients who cannot digest milk. Farinaceous foods and sugar predominate in his diet scale; potato *purées*, light soups, semolina cakes, fruit jellies and fruit juice, with cocoa and butter. He does not give milk till convalescence, when he also gives eggs, and then meat. He adds after some time to his diet cultures of the paralactic bacillus.

Thomson, in cases in which the temperature is not high, suppresses the milk or reduces it considerably, adding meat juice, lactose, white of egg, and light broths. In the first days of apyrexia, if the patient has no diarrhœa or distension, and has not had hæmorrhage recently, his diet-scale consists of pastry, sweets, lightly-cooked eggs, rice, milk, biscuits, mutton or chicken broth, meat jellies and farinaceous soups. The doctor can modify the diet according to the indications furnished by each particular case. He should only remember that the diet of the typhoid patient must be at once substantial and perfectly assimilable, that all the digestive secretions are deficient in these patients, and that one must not force upon them a diet which cannot be easily digested; that it should not contain any solid particle which is capable of

mechanically irritating the intestine; and that, finally, it should not be distasteful to the patient, who has already too great a tendency not to take enough nourishment.

Antipyretic Measures

One of the first indications in typhoid fever is to lower the temperature. This result may be obtained by external applications or internal treatment.

External applications comprise a certain number of hydro-therapeutic measures, such as *affusions*, *wet packs*, *sponging*, *baths*, applications of ice, compresses and enemata.

Sponging.—Sponging, which was introduced by Jaccoud, can easily be employed at any time or place, and may be sufficient in the treatment of slight or moderate attacks. According to O. Martin, intestinal hæmorrhage, myocarditis, or a tendency to collapse should contra-indicate its use, but Milhit, on the contrary, says that sponging is indicated in all syncopal or hæmorrhagic forms. Pulmonary complications are not a contra-indication. They may be given with cold (53·6–59° F.) or warm water. The duration of the sponging must not exceed three minutes; the colder the water the shorter it must be. The patient lying at full length naked on the bed, a large sponge is rapidly passed all over his body, soaked with water which is either plain or, better still, contains eau de Cologne or aromatic vinegar. The patient is then rolled in a blanket and given a hot alcoholic drink. He is left thus for fifteen to twenty minutes, and then wiped without touching the abdomen. Two to ten or twelve spongings may be given in this way as a substitute for baths.

Although its action on the temperature is very slight, sponging is nevertheless extremely useful owing to the sense of comfort which it induces as a result of the sedative influence on the nervous symptoms and the stimulating action on the prostration.

Affusions.—Affusions are an old-standing practice,

having been introduced by Currie and employed in France by Récamier, Chomel, Trousseau, Guéneau de Mussy, etc. Contra-indications to their use are the same as in sponging, or even stronger. Besides, patients do not support them well. Baths are to be preferred if a fall of the temperature is desirable. "The patient is placed in a bath, and two persons in rapid succession pour cold water of 50–59° F. on his head and back for some minutes; if a douche is available, its duration should be very short, and not exceed one to two minutes" (Guéneau de Mussy). The fall of temperature obtained is on an average 0·9–1·0° F.

Wet Packs.—Wet packs, consisting of a moistened sheet, are to be recommended chiefly for children. They calm restless patients and make them sleep. Their technique is simple. A sheet is plunged into cold water, wrung out vigorously and spread on a blanket. The patient is placed naked on the sheet and wrapped up completely in it. He is left thus for about a minute, then wiped and put back to bed. This method of reducing the temperature is a rather brutal one. It causes a shock to the typhoid patient and provokes intense distress, and sometimes even syncope.

Treatment by baths.—Balneotherapy is the treatment of choice in typhoid fever. Not only does it cause a remarkable fall in temperature, but by its remote effects especially it possesses a very real and efficacious therapeutical action. The most certain and best studied of these effects are: improvement in the pulse and arterial tension, which indicate improvement in the cardiac tone; calming of the nervous symptoms; increase in diuresis and the intestinal secretions; diminution of the dryness of the mouth and stimulation of respiratory oxidation.

Brand's method.—Currie (1787) introduced this method, which Brand (1861) appropriated and codified, and Glénard (of Lyons) introduced into France. Brand's complete method consists in giving the patient, night and day every three hours, a cold bath for a quarter of an hour at 64·4° F. if the rectal temperature

is above 102·2° F. To attenuate the disagreeable impression caused by the first bath, it may be given at 71·6° F. The following baths are each lowered by 1·8° F., so that the fifth would be at the desired temperature of 64·4° F. (Brand, Juhel-Renoy).

Cold affusions are given by pouring water at 50° F. on the nape of the neck from just above the head for two minutes each time.

Tripier and Bouveret recommend continuous affusion.

As soon as the patient enters the bath he is given a drink of brandy or wine. About ten minutes after the commencement of the bath he is seized with intense shivering. This is the signal for the bath to end. He is given another drink of brandy or wine and placed at full length on the bed, on which has been previously laid a blanket covered with a warm dry sheet. He is then wiped quickly and gently without touching the abdomen, wrapped up in a blanket, with a hot bottle at his feet, and left to *shiver*. In a quarter of an hour or half an hour's time general relief is experienced. The patient feels better, and after he has been clad and given a drink he usually goes to sleep.

In severe hyperpyretic and adynamic fevers in which the heart, kidneys and lungs are severely affected, the advocates of Brand's method employ a special technique until improvement sets in, called the *intensive method*, of which Juhel-Renoy gives the following description. A first bath is given at 78·8°, a second at 75·2°, and so on, diminishing each bath by 3·6° F., so that by the eighth bath the regulation temperature of 64·4° F. is reached. The duration of the bath will be shorter: eight to ten minutes. Shivering is to be *obtained* and *prolonged* by lowering the temperature of the bath to 59·0°. Cold affusions (46·4–50° F.) should be carried on throughout the duration of the baths, with massage and friction of the limbs under water. Large thoracic and abdominal compresses are absolutely necessary. If the patient shows the least sign of getting worse he should be put in a bath again every two hours instead of every three hours, and if the heart

shows signs of weakness, an ice-bag should be placed on the præcordial region.

Such is Brand's method, which involves no form of treatment besides the baths. According to its advocates, its only contra-indications are profuse intestinal hæmorrhage and perforation.

A method of this kind rigorously carried out is not suitable for all patients, and especially for women and children, or nervous and impressionable patients, or for soldiers coming from the trenches exhausted both by the infection and overwork. In a hospital where the best installation and nursing were available, it yielded a mortality of 19·5 per cent. (Petges, Dumora and Peyri). Whatever may be its advantages, in ordinary cases equally good results may be obtained by milder methods which are less disagreeable to the patient.

Warm or tepid baths (89·6–82·4° F.), which constitute a mild form of Brand's method, regulate the temperature curve in the same way.

Nervous and excitable patients, as well as children, support them better than cold baths and derive more marked benefit therefrom. These baths may be of short duration—ten minutes, for example, with or without cold affusions on the nape of the neck at the end of the bath (Grasset)—or be prolonged even for a whole day (Riess).

Warm baths gradually chilled.—In the chilled bath the advantages of the cold bath are retained without those properties which are unnecessary or disagreeable to the patient. This method was introduced by Bouchard, who uses a bath whose temperature is 3·6° F. below that of the patient. By adding cold water the bath is gradually refrigerated by 1·8° F. every ten minutes. When the water is at 86° F., the chilling is stopped, and the patient is taken out of the bath. The higher the temperature of the patient, the longer these baths may be continued. They are repeated six to eight times in the twenty-four hours. Carrieu reduces the duration of the bath to a maximum of an hour, starting with a temperature of 98·6°, and chilling

it sometimes more rapidly by adding cold water every five minutes until it reaches 86·0°.

He gives five or six baths on the average; often less, rarely more, being guided by the initial temperature for the day. If three hours after a bath the patient's temperature has not fallen by 1·8° below his initial temperature, he gives another bath; but if it has, he waits an hour or more.

In some forms of typhoid fever, with hyperpyrexia and nervous phenomena, cold baths, which should be repeated as often as is necessary, still constitute the real treatment. It is most important not to delay, and to employ them *from the beginning of the disease*, regulating the number of the baths by the patient's temperature.

Hot baths.—Bosc advocates hot baths at 102·2° F., and from twelve to fifteen minutes in duration. They gave him good results in the treatment of cholera, as well as in severe broncho-pneumonia and bronchitis. According to him, these warm baths have an eliminatory, sedative, revulsive and antiphlogistic action, as well as a regenerative effect upon the myocardium. Bosc recommends them for children who violently object to cold baths, and for cases with grave respiratory complications, anuria or diminution of the urinary secretion, severe delirium, or when the heart is much affected. In the adult "the two most formal indications—*i.e.* those in which no other method can be permitted—are (*a*) in cases where the cold bath is contra-indicated owing to the state of the heart; (*b*) in the case of the hæmorrhagic form of typhoid fever, and especially in hæmorrhagic nephritis with headache, nausea and vomiting, suggesting an uræmic complication" (O. Martin).

Whatever the mode of bath treatment adopted, there are certain rules which must always be followed. *The patient should not make any effort.* He should be carefully carried from his bed to the bath, which should be near at hand, in the same room. He should never, in any case, go there by himself, owing to the

risk of intestinal perforation, syncope or sudden death. The water in the bath should be changed very often, at each bath if possible, or at least once in the twenty-four hours. The patient's buttocks should be slightly vaselined before the bath. Grave infective complications may sometimes originate from baths given with water contaminated by fæces, and the water should have a mild antiseptic put in it (boracic acid, cresyl, naphtholate of soda, liquor sodæ chlorinatæ).

Advantage should be taken of the bath to clean the patient's mouth and give him a warm drink systematically. The typhoid patient should never be left alone, even for a minute, during the bath. In some cases the doctor should give the bath himself, and carefully watch the pulse meanwhile.

On leaving the bath, the patient should never be rubbed down or wiped dry. He should be put on his bed wrapped up in a blanket, and the reaction should be waited for. The beginning of the phase of reaction is an indication for giving him another drink. If this phase is too prolonged or is unsatisfactory, the patient should be warmed by hot drinks, and given coffee, and the following bath must be shorter and hotter.

There is an absolute contra-indication if intestinal perforation or commencing peritonitis is suspected. If there is considerable intestinal hæmorrhage which is repeated, the baths should be stopped for a few days and then resumed, a careful watch being kept upon the patient, or cold sponging should be substituted.

Baths should also be discontinued if phlebitis occurs. The appearance of a cardiac complication requires the presence of the doctor during the bath, so as to guard against a possible fainting attack.

With these exceptions, baths have no other serious contra-indications; they should not be prevented by pulmonary congestion, bronchitis or menstruation.

Compresses.—Brand borrowed from Jacquez (of Lure) the method of *cold water compresses*, which are placed on the abdomen, thorax, head and even the whole body, and frequently changed. Cheinisse recom-

mends the direct application to the abdomen of a compress soaked in 90 per cent. alcohol and wrung out. The compress is covered with a layer of wool soaked in cold water, on which is placed a piece of mackintosh, and the whole is kept in position by a flannel bandage. The water compress is changed every hour, and the alcohol compress every two hours.

Enemata.—In 1875, Foltz (of Lyons) proposed the administration, every three or four hours, of a litre of cold water of a temperature of 50–59° F. *per rectum.* Nowadays large injections or enteroclysis are preferred, consisting of three to four litres at a low pressure by the use of a sufficiently long tube. Two enemata of boiled water are given daily at a temperature of 64·4–68° F. if preferred cold, or at 104–107·6° F. if hot. Hot enemata appear to be more diuretic than cold, though the latter, on the other hand, bring down the temperature more. Whether cold or hot, they clear the intestine of débris and putrid products, allow the absorption of fluids, and may serve as a vehicle for antiseptics which will disinfect the lower part of the intestine. Thus to the boiled water can be added boracic acid, phenosalyl, in doses of 5 grammes per litre, or liquor sodæ chlorinatæ, in doses of 10 grammes per litre.

Drop by drop method.—The intra-rectal instillation of a solution of glucose or cane sugar in a strength of 50 or 60 per 1000, drop by drop, gives excellent results, rapidly causes the headache and general discomfort to disappear, and at the same time increases the urinary secretion (P. Emile Weill, F. Rathery, J. Carles, etc.). It should be given hot (122° F.) and very slowly. Three hours at least are needed for the instillation of a litre of fluid. Under these conditions only can the patient keep and absorb the fluid. If necessary, adrenalin or chloral can be added to the sugar solution.

Refrigeration by cold air.—J. Sabrazès has had recourse to refrigeration of the typhoid patient by cold air, thus reviving the simple, practical and efficacious method of James Sims (1778).

Internal medication.—Generally speaking, *as few drugs as possible* should be given in typhoid fever. They fatigue and irritate the stomach, sometimes provoke vomiting, and, with the exception of special and definite cases, are of little service (Lemoine and Gérard, Dieulafoy). As regards the antipyretic drugs which have been recommended, we will say a few words about those most commonly employed.

Cryogenine should be used only when the urine is abundant. Apart from its antipyretic action, it is analgesic, and causes the headache to disappear entirely. The dose for an adult is 0·30 gramme. It is well to know that it colours the urine yellow, and that some typhoid patients suffer from severe hypothermia, with collapse, even after 10 centigrammes of the drug.

Pyramidon, even in very small doses and combined with caffeine, may cause profuse greenish vomiting, with pronounced contraction of the abdomen and a fall of temperature to 98·2°, suggesting perforation (Hirtz); it may also produce severe symptoms of collapse (Rist, Brault).

Antipyrine, whether combined or not with bicarbonate of soda, has an injurious action both on the heart and kidneys; it diminishes the elimination of toxic products. These two drugs, therefore, should not be generally employed.

Quinine should not be used for lowering the temperature. It has no antipyretic action in the course of the disease. It may be employed as a tonic (Robin, Lemoine and Gérard). It is best to reserve it for those cases in which the history or examination of the blood shows that the patient is the subject of malaria. Marfan has advocated it on account of its stimulating action on the heart, especially in children : the hydrochlorate of quinine is the preparation chiefly used, in doses of 0·05 gramme to 0·10 gramme for each year of age, in the twenty-four hours, and in doses of 0·50 to 1 gramme in adults.

Various Modes of Treatment

Bleeding.—Bleeding, of which so much abuse was made in former times, may serve as one of the agents for combating infection (Pecker, Grasset, O. Martin). It may be employed in the severe forms in which the patient presents marked signs of intoxication; such as a very pronounced typhoid state, or in the ataxo-adynamic form; likewise in cases in which the patient has a severe attack with a feeble reaction and comparatively low temperature.

Lastly, it will be prudent to bleed if other methods for removing toxins are not sufficiently rapid; when the heart-sounds become more and more muffled and the pulse weak, soft and irregular with a high number of beats, 150, 200 or 300 grammes of blood may be withdrawn, but an injection of *artificial serum* should be made at the same time. The solution employed will be the so-called normal saline solution of sodium chloride at 7 per 1000 (Dastre, Mayet, Delbet, Bosc and Vedel). Dieulafoy adds 0·10 gramme of benzoate of caffeine per litre of serum to 9·5 per 1000 of sodium chloride, and injects from 50 to 400 grammes. The injection may be made into the muscle, but if it is made after the bleeding, or if rapid effect is desired (*e. g.* in a case of alarming collapse), it should be made intravenously and very slowly. Injections of normal saline raise the blood pressure, stimulate the nervous and hæmatopoietic centres, and facilitate the elimination of toxins by provoking abundant diuresis, frequent diarrhœa and sometimes vomiting.

Fixation abscess.—This old method of treatment, which has been employed with varying success for the treatment of septicæmia, consists in the injection of 1 c.c. of oil of turpentine beneath the skin of the thigh on its outer aspect. It is said to cause a decided fall in the temperature and improvement of the patient's general condition if it results in the formation of an abscess (Rathery). When the injection does not cause an abscess, the prognosis as a rule is gloomy. J. Carles

usually keeps this method for septicæmic forms with severe and protracted broncho-pneumonia, and for those occasions in which a serious inflammatory or purulent localisation may be expected owing to the organ affected.

Antiseptic medication.—For the digestive disturbance which is so pronounced a feature at the onset of typhoid fever, hydrochloric lemonade may be of service in doses of 2–4 grammes per litre.

Purgatives and laxatives should not be employed either in the adult or child, except in the course of the first week. At the onset a saline purgative may be given, *e. g.* 15–20 grammes of sodium sulphate or magnesia : calomel, whose action on the liver is well known, may be given, especially to children. Dieulafoy employs manna in doses of 15–25 grammes in milk.

After the first week every purgative or laxative should be avoided, as they are capable of producing just those complications which we endeavour to avoid, viz. hæmorrhage, perforation and peritonitis. If their employment does not always have such grave results, it may cause rises of temperature. Courtellemont has fairly often seen death from perforation, especially from the twelfth to the twentieth day, after the administration of a purgative. The following course of events is not uncommon : the taking of a laxative or purgative, two days afterwards hæmorrhage, and two or three days later perforation and death.

Among other drugs employed, the most usual are *beta-naphthol*, in doses of 2·50 grammes in the twenty-four hours (Bouchard); *betol* (salicylate of naphthol); *benzonaphthol*, 3–4 grammes in 6 or 8 doses suspended in milk; *salol*, associated or not with *salicylate of bismuth* (Dujardin-Beaumetz); *lactic acid* in the form of lemonade in doses of 15–25 grammes daily (Hayem); *peroxide of magnesium* in keratinised capsules of 0·30 gramme, two capsules to be taken every three or four hours (Kirkpatrick); *camphorated phenol* in doses of ten drops every two hours; *urotropine* (Chauffard, Triboulet and Lévy), which, it must not be forgotten, may

cause hæmaturia in acute infectious diseases, and especially in typhoid fever (Karkowski), but, by reason of its elimination by the bile passages, causes a biliary and genito-urinary antisepsis simultaneously. *Iodine*, as the freshly prepared tincture, has been employed by Raymond, Arnozan and Carles.

Diuretics.—We have already insisted on the necessity of making the typhoid patient drink a large quantity of fluid, so as to provoke diuresis, and elimination of all the toxins by the renal channel.

Injections of normal saline favour diuresis. It is the same with *cold sponging, baths* and *hot enemata*. These different methods will suffice in most cases. It may, however, be necessary to prescribe *lactose, theobromine, digitalis* and *adrenalin*, which have a diuretic action, but also respond to other indications.

Tonics.—*Alcohol* in all its forms (wine, rum, cognac, liqueurs) is a good tonic. English physicians give doses of alcohol which we regard as excessive, sometimes more than a litre in the twenty-four hours. In France an average of 80–100 grammes of alcohol is given. Frequent use is made of wine, chiefly champagne, which the patients tolerate and drink readily, especially when it is iced.

Caffeine and *ether* respond to special indications, which we will discuss later.

Drugs for combating infection.—The direct employment of colloidal substances has been proposed, *e. g. collargol*, electrargol, lantol (colloidal rhodium), colloidal gold (Letulle). Their action in some cases has appeared beneficial, but their value is by no means proved. Robin, who has paid special attention to the study of electrargol and collargol, concludes that they are inefficacious in the treatment of typhoid fever.

Treatment of Complications

In the course of typhoid fever certain normal symptoms may become exaggerated and constitute an aggravation, such as diarrhœa when it becomes pro-

fuse and does not yield to treatment. But these are mere incidents. The real complications are "intestinal hæmorrhage and perforation, pulmonary congestion and pneumonia, myocarditis and weakness of the heart, nephritis, and every result of the lesions, degenerations and infections peculiar to typhoid fever of a severe character or which has come under treatment late" (Merklen). These accidents and complications involve special indications for treatment, which we will briefly describe.

Complications Involving the Digestive System

Diarrhœa.—Too active measures should not be taken against the diarrhœa. To check it, it will be sufficient to give sterilised milk diluted with lime water, or to lengthen the interval between the feeds.—Lemonade with *lactic acid* (10 grammes) with syrup of rhatany or lemon, benzo-naphthol, *salicylate or subnitrate of bismuth,* absorptive powders such as prepared chalk and charcoal, or *dermatol* (subgallate of bismuth) may be prescribed.

Constipation.—Avoid laxatives and purgatives after the first week. Have recourse to *intestinal lavage* or enemata. A daily enema of boiled water, which may be given cold (when it does not cause colic) or warm, is usually sufficient. Emollient enemata (mallow, or marsh mallow root) have been recommended. Oil or glycerine may be added to the water. When the constipation is obstinate, and accompanied by abdominal pain and meteorism, calomel (10–25 centigrammes) should be given.

Vomiting.—This may sometimes be due to too large a consumption of alcoholic beverages, and their diminution or suppression will be enough to stop the vomiting. Iced or aerated drinks, and cold compresses or ice on the epigastrium will also produce a good result. Hydrochloric lemonade (2–4 grammes per 1000), *Rivière's potion, ether* sprays, inhalations of *oxygen* and *menthol*

(in three or four doses of 5 centigrammes at long intervals) will give good results. Vomiting is fairly frequently a symptom of suprarenal insufficiency, as is proved by the efficacy of treatment by adrenalin (Khoury).

Intestinal hæmorrhage. — Absolute rest should be ordered. The baths must be stopped; the patient should be placed in the dorsal decubitus with an ice-bag on the abdomen; drinks should be iced and in very small quantities, consisting of champagne, iced lemonade with eau de Rabel, or a draught containing water 130 grammes, syrup of rhatany 30 grammes, eau de Rabel 2 grammes (Dieulafoy), to be given in spoonfuls.

Every twenty-four hours the patient should be given 3–4 grammes of calcium chloride, with or without large hot enemata (Mathieu).

If the hæmorrhage is profuse and obstinate, all food by mouth should be absolutely stopped, and an injection of *normal saline* (600 c.c.–1800 c.c.) should be given at a temperature of 102·2 or 104° F.

Injection of gelatinised serum has given good results. The hæmorrhage may be so profuse that the patient faints. In that case the head should be placed as low as possible, an injection of ergotinin should be given, and then as soon as possible an injection of horse serum or normal saline solution. The patient should be made warm. Injections of *camphorated oil* and *ether* are sometimes of service.

Intestinal perforation. Peritonitis. — "Every undoubted perforation of the intestine demands surgical intervention" (Michaux). This intervention should be done as soon as possible. While waiting for the surgeon, the patient should be kept absolutely still in bed, all fluid should be stopped. An intramuscular injection of nucleinate of soda should be given (Miculicz, Chantemesse, Tuffier), which has the property of causing a leucocytosis which increases the patient's resistance. If necessary, injections of ether, camphorated oil or caffeine should be given.

The physician's rôle is limited to this. Surgical intervention alone can save the patient.

Cardiac complications.—In moderate attacks the strength of the heart is, as a rule, sufficiently maintained by the diet, meat juice, etc., containing alcohol and wine. In more severe attacks ice should be put on the præcordial region, the baths should be given hotter and with extreme care, at longer intervals or stopped altogether. Repeated injections should be given of camphorated oil, ether, sparteine, sulphate of strychnine, and normal saline solution containing adrenalin. Lastly, since the rôle of the suprarenals has been better understood, numerous accidents due to suprarenal insufficiency have been reported (E. Sergent, Hutinel). The patient is given adrenalin subcutaneously, either in the form of $\frac{1}{4}$–$\frac{1}{2}$ c.c. of a 1 in 1000 solution, or, better still, as adrenalin in a saline solution obtained by adding 1 c.c. of 1 in 1000 solution of adrenalin (*i. e.* 1 milligramme of adrenalin) to 250–500 c.c. of normal saline solution (Josué).

The total extract of the suprarenals taken internally in daily doses of 0·20 to 0·40, with or without injection of normal saline solution with adrenalin, glucose or novocain, is very successful in the severest cases with threatening collapse, or at the time of convalescence (Rathery, Josué, Sabrazès).

In some cases faradisation of the heart has been employed with success, the positive electrode being placed on the pneumo-gastric and the cathode over the heart.

Pulmonary complications.—Pulmonary complications are far from being a contra-indication for baths. At most they may sometimes have to be given a little hotter. It is most important for the typhoid patient to change frequently his position in bed. This change will prevent or restrict any pulmonary complications. If they do occur, *dry or wet cupping* will be the best treatment. Blisters should never be applied.

In cases of diffuse bronchitis or broncho-pneumonia, injections of emetine hydrochloride for four consecutive

days, in doses of 4, 6, 7 or 8 centigrammes, have given the most excellent results.

Serous or hæmorrhagic pleurisy is generally absorbed and very rarely requires thoracocentesis. As for *purulent pleurisy*, if thoracocentesis is not sufficient, it may be necessary to perform thoracotomy. If the laryngeal symptoms do not yield to moist, hot compresses or inhalations, in severe cases with suffocative attacks it will be necessary to resort to tracheotomy.

Nervous complications.—Hot or cold baths exercise a remarkably sedative action on most nervous symptoms. These may, however, by their intensity and obstinacy, require special treatment.

Headache is usually diminished or removed by affusions, or cold or iced compresses, but sometimes proves more obstinate. Lumbar puncture not only permits of examination of the fluid withdrawn, but causes almost immediate relief. A single puncture is often sufficient.

Urinary complications.—When the patient passes little urine, dry cups should be placed over the kidneys. But the best diuretics are always the cold bath, milk and lactose. Diuretic drugs have generally little effect. If the patient has retention, he must be catheterised, with the aseptic precautions described above.

In cases of bacteriuria the bladder should be washed out with a weak solution of permanganate of potash.

Cutaneous complications.—In dealing with the nursing of the typhoid patient we have laid special stress on the skin lesions, which can be prevented by asepsis. If a *bedsore* develops, in spite of all the precautions taken, it should be disinfected carefully and closely watched, for it may be the starting-point of secondary septicæmia.

In addition to the measures indicated above, we may use dressings of salol, aristol, dermatol or Vincent's antiseptic powder (boracic powder 100 grammes, fresh hypochlorite of calcium 10 grammes).

Abscesses and *phlegmons*, especially in the *parotid*, should be incised without delay.

Specific Treatment

Serum therapy. Vaccine therapy.—A successful specific treatment for typhoid and paratyphoid fevers has long been sought for. Two methods have been proposed: *Serum therapy* and *Vaccine therapy.*

Serum therapy.—Chantemesse has employed a serum derived from horses which have undergone a long immunisation. These horses were given *soluble typhoid toxin* exclusively. At present, injections of this toxin are sometimes given and sometimes intravenous injections of living bacilli, according to the method of Rodet and Lagriffoul.

Soluble toxin is obtained by cultivating very virulent typhoid bacilli on a special medium containing defibrinated blood and spleen and bone-marrow broth (Chantemesse). In a week's time the culture is heated to +.55° C., centrifugalised and decanted.

The most active serum is obtained after the last injection given to the horse. But the activity of this serum varies.

At first Chantemesse injected the patient with 5–15 c.c. of his serum, but later he injected extremely small doses, consisting of only a few drops.

According to Milhit, the serum stimulates the organs producing *opsonins*, the secretion of which becomes very intense. At the same time a high leucocytosis appears (as much as 18,000 white cells per cubic millimetre), with polymorphonucleosis and eosinophilia (Balthazard).

According to Chantemesse, the worse the patient is, the smaller should be the doses of serum injected. He particularly advises that cold bath treatment should not be neglected, but continued with the serum treatment. From statistics published by him and by Josias and Brunon, it appears that the mortality in cases treated by this method has been 4·3 per cent.

A large number of serums has been prepared by injecting animals with filtered cultures (Shaw, Meyer, Bergell, Aronson, Richardson, etc.), or extracts of

bacilli ground in liquid air (Macfadyen). Besredka inoculated an animal first with dead and then with living bacilli. Jez has used the blood-forming organs (bone-marrow, spleen, thymus), in a crushed and filtered state, from animals which had been strongly immunised against the typhoid bacillus. H. Vincent prepared a typhoid serum by injecting a horse with very virulent and highly toxic cultures of strains of bacilli cultivated in a collodion bag within the peritoneum of a guinea-pig.

Rodet and Lagriffoul inject living cultures of bacilli into the veins of sheep and horses. According to them, the most active serums are derived from animals who have received only a small number of injections and minimal doses. Serums derived from animals who have been given too large and numerous doses have an injurious effect, and even show an action which favours the experimental toxi-infection. Rodet thinks that the treatment by this serum should only be undertaken when typhoid fever has been diagnosed by a blood-culture or serum test, without any previous or super-added infection. Myocarditis and intestinal hæmorrhage form absolute contra-indications. The serum should be given subcutaneously, at an early date, *i. e.* at the latest at the tenth to the eleventh day of the febrile period; 15–20 c.c. are given at one or two injections, with an interval of two days.

According to Rodet, in thirty-six to forty-eight hours a fall of temperature, improvement of the general condition, and, in spite of the high temperature, a marked sense of well-being are to be observed. In patients who have not had the bath treatment there is a veritable polyuria, which precedes apyrexia by several days. In several cases the disease is shortened. The writer recognises that "the result depends on the quality of the serum, for it is difficult to make the horses produce a serum whose value is constant."

Vaccine therapy or *bacterial therapy*.—For the first time, in 1892, Frænkel treated fifty-seven patients by injecting them with cultures of typhoid bacilli which

had been heated to 63° C. (in doses of 0·5 c.c.–2 c.c). He had five deaths, or a mortality of 8·7 per cent.

Since then numerous authors have employed vaccine treatment by various methods, in England (A. E. Wright), in the United States (Petrovitch), in Italy, etc.

The vaccine used for this treatment may be divided into three classes—

1. Vaccines of living bacilli.
2. Vaccines of bacilli killed by heat.
3. Vaccines of bacilli killed by ether: Vincent's bacillary vaccine and autolysat.

1. *Vaccines of living bacilli. Living sensitised vaccine* (Besredka).—This vaccine, when given in four injections in increasing doses, one every three days (in doses of from one to four thousand millions), produces locally pruritus, more or less marked erythema, with decided rise of temperature and improvement of the general condition in twenty-four to forty-eight hours, with marked diurèsis and sometimes actual polyuria. Some days later there is a progressive fall of the temperature. Ardin-Deltheil, Nègre and Raynaud have employed it in thirty-seven cases in patients who were having the ordinary general treatment. They had no deaths, and only two of their patients had relapses.

Sablé thinks that Besredka's vaccine has in some cases produced an undoubted action on the temperature and general condition. Deléarde and Leborgne, who have employed it in the typhoid fever of children, do not think that the old methods of treatment should be given up at present, *e. g.* cold baths, ice to the præcordial regions and plenty of fluids.

Faucher and Lafosse have had rather bad results with this vaccine in military patients.

2. *Bacilli killed by heat.*—Josué and Belloir have made use of autovaccines, *i. e.* vaccines obtained from cultures of bacilli derived from the patient himself and heated to 56° C. for six hours. They give three injections of 200,000,000 bacilli at twelve hours' interval. They say that they have obtained good results, without any complications.

The other vaccines in use are mostly hetero-vaccines.

Among these is the *bacillary vaccine* sterilised by heating at 56° C., used in England, the United States, etc., as well as in France. The vaccine to be employed contains, on the average, 100,000,000 bacilli per c.c.

The injection is made in the deltoid region. At the onset of the disease, in severe cases, small doses must be given. The first injection is thirty, forty, or fifty million bacilli; the second, given five days later, is half the first, and the third and fourth, given at the same intervals, are only ten millions.

The temperature curve descends regularly by lysis after treatment. D'Oelnitz, in children, obtained similar results, with leucocytosis and definite increase in the size of the spleen. Castaigne has published a series of charts showing rises of temperature after each injection of vaccine. These rises were followed by a pronounced fall the next day.

Generally speaking, heated bacillary vaccines employed in large doses have a violent action, which cannot be measured or foreseen. The reaction of the temperature in an upward or downward direction is often very marked. A certain number of writers are guarded as to their use, as it may be accompanied by shivering, collapse, icterus and even rupture of the spleen. But such accidents are the result of too large doses.

In order to avoid subcutaneous injections, Courmont and Rochaix have suggested giving patients two rectal injections daily until convalescence, containing 100 c.c. of a culture of typhoid bacilli killed at + 53° C.

3. *Polyvalent bacillary vaccine sterilised by ether. Autolysat.*—H. Vincent has shown that the preventive vaccine tends to check the disease if it is given at the onset of the incubation period, when the exact moment at which the ingestion of typhoid bacilli took place can be determined (laboratory cases). It has also been found that individuals vaccinated during the incubation period have had mild, abortive or shortened attacks of typhoid fever.

Generally speaking, considerable prudence is required in the employment of vaccine therapy, the object of which is to rouse and stimulate the latent defensive forces of the infected organism and to provoke the secretion of an excess of antibodies (amboceptor, bacteriolysis, etc.).

The indications and contra-indications for vaccine treatment by the ether vaccine may be resumed as follows—

1. A patient with a severe attack, and especially one of long-standing, should not be given vaccine treatment. He cannot undergo with impunity the shock necessarily induced by the inoculation of an additional quantity of antigen. It is, therefore, at the beginning or in the first two weeks of the disease—when the patient still possesses a store of defensive energy and is not too deeply intoxicated—that vaccine treatment can be employed to best advantage.

2. Too high doses of antigen may be dangerous. It is evidently just the same with anti-typhoid vaccine as with any very active drug. But, on the other hand, too small doses, whether repeated or not, remain without effect.

Experience has shown that extracts or autolysats of living bacilli, afterwards sterilised by ether, produce in the adult very superior results to those given by the bacillary vaccine properly so-called. The latter, on the other hand, has yielded remarkable results in the child (E. Weill).

Bacillary vaccines and specific autolysats sterilised by ether are prepared for typhoid fever, and for paratyphoid A and B fevers.

Before undertaking vaccine treatment one should make sure of the diagnosis by an early cultivation of the blood. In the absence of a blood-culture, investigation of the spleno-reaction, carried out with the autolysat (it is very inconstant with the bacillary vaccine), may help to settle the diagnosis.

The first dose of antigen to be injected in an adult is 1 c.c.

The inoculation is made subcutaneously in the clavicular region (and not behind, as in preventive inoculation), because the patient is in bed. The injection should be made preferably in the morning. If the vaccine causes an abnormal rise of temperature or pain, 0·50 gramme of aspirin should be given an hour after injection, except in cases of intolerance or special contra-indication.

If the temperature does not fall thirty-six or forty-eight hours later in an appreciable degree, the injection may be repeated, when the spleen, which had become enlarged, has returned to its former size. This reduction in size usually occurs two or three days later. The dose on the second occasion is 1–2 c.c. However, if a fall of temperature occurs, one must avoid disturbing this salutary defervescence by a fresh injection of vaccine. Such an injection would result in arresting the decline of the fever, and in causing a sort of negative phase by neutralisation of the already existing amboceptors. Another injection should only be made when the temperature has returned to its former level, or nearly so.

Very marked enlargement of the spleen constitutes a contra-indication for the use of vaccine treatment (Vincent).

In patients treated by vaccine therapy there is no need to modify or suspend the cold bath treatment.

The injection of vaccine causes, or may cause, a diminution of the toxi-infective symptoms, and, two or three days later, a fall of the patient's temperature. Convalescence may occur in two, three or four days. Unfortunately, this improvement in the symptoms is *by no means constant.*

Relapses seem rarer than in patients who have not been treated by vaccine.

Variot, Grenet and Dumont have treated sixteen patients with Vincent's polyvalent vaccine. Only one died, and he had been injected at the time of a perforation. Four times defervescence was obtained in twelve days. In one patient, in the course of a severe

relapse with meningeal symptoms and infective erythemata, the temperature fell in forty-eight hours after an injection of 1 c.c. of vaccine. In the other case the duration was shortened, the general state improved, and the pulse rate lessened.

In thirty-four out of fifty cases treated by Thiroloix the disease was made milder and shorter.

E. Weill treated fourteen children by the preventive bacillary vaccine, sterilised by ether. These cases of typhoid fever, which were of moderate intensity, first came under treatment from the third to the tenth day.

Weill injected children above five years of age daily with $\frac{1}{4}$ c.c., $\frac{1}{2}$ c.c. and 1 c.c.; then, after missing one day, with 1·5 c.c. and 2 c.c. Below that age he began with $\frac{1}{8}$ c.c., to end with 1 c.c. or 1·5 c.c.

Recovery was obtained in one or two weeks, in one case only in twenty days. There was no death, no relapse and no complication.

Lenglet treated his paratyphoid A cases with vaccine therapy. Although it did not always reduce the duration of the height of the disease, the vaccine seemed to prevent any relapse. Doubtless for the same therapeutical reason complications were exceptional.

Rathery and Michel treated with Vincent's autolysat para. B 147 cases of paratyphoid fever B, in which the diagnosis was confirmed by laboratory examination. They had only five deaths, or a mortality of 3·40 per cent. They regard vaccine therapy as a useful adjunct to treatment, a very definite improvement of the general state having followed the injections almost invariably. In a fairly large number of cases the disease seems curtailed, and the symptoms of a hurried crisis occur (fall of temperature, polyuria, etc.).

In some subjects vaccine therapy seems to produce no perceptible effect, but even in these cases it seems that the method of treatment does not fail to exercise a beneficial influence on the course of the disease.

P. Emile Weill has treated some cases of obstinate typhoid osteomyelitis by injections of H. Vincent's ether vaccine, with excellent results.

The treatment consists in two injections weekly until recovery: the doses of the first injections are respectively $\frac{1}{4}$ c.c., $\frac{1}{2}$ c.c., $\frac{3}{4}$ c.c. and then 1 c.c., which dose is then continued without further increase. When employed in this sort of preventive manner, vaccine therapy will yield remarkable results, considering the slowness with which the typhoid bone lesions form.

In osteomyelitis of paratyphoid origin, Weil thinks it would be advisable to employ the same method, using paratyphoid bacilli.

SECOND PART

EPIDEMIOLOGY AND PROPHYLAXIS OF TYPHOID FEVER AND PARATYPHOID FEVERS

CHAPTER VI

EPIDEMIOLOGY OF TYPHOID FEVER—FREQUENCY OF THE DISEASE

THE historical and geographical study of the epidemic or endemic manifestations of typhoid fever bears witness to the extent and gravity of this important disease. No country is protected from its attacks. It is prevalent in villages as in large towns, in armies in time of peace and still more so in time of war, when it causes a considerable number of deaths.

In France, in the course of twenty or twenty-five years, typhoid fever carries off a number of inhabitants equal to that of a large town such as Toulouse. From 1906 to 1910 (both inclusive) *The Sanitary Statistics of France,* published by the French Home Office, registered 22,463 deaths due to this infectious disease. During the same period of four years Paris alone had 1251 deaths from typhoid fever.

From 1891–1900 the average proportion of deaths from typhoid fever per 100,000 inhabitants in some of the towns of France has been as follows—

Havre	115	Rheims	30
Rouen	61	Lyons	24
Marseilles	56	Bordeaux	24
Nantes	45	Paris	21
Toulouse	32	Lille	11

The deaths from typhoid fever in France from 1913 to 1915 inclusive, in towns of 30,000 inhabitants and more, have been as follows—

1886–1890	0·54	per thousand
1891–1895	0·34	,,
1896–1900	0·30	,,
1901–1905	0·20	,,
1906–1910	0·18	,,
1911	0·18	,,
1912	0·13	,,
1913	0·14	,,

From 1896–1900 the typhoid mortality in the principal European countries reached the following figures per 100,000 inhabitants—

Italy	49·7	Sweden	15
Hungary	34·4	Denmark	11·1
France	27·6	Germany	10·3
Belgium	25·8	Netherlands	10·2
Austria	24·6	Switzerland	8·4
Ireland	20·7	Norway	7·5
England	17·5		

More recently, the comparative mortality from typhoid fever in various European countries per 100,000 inhabitants has been as follows—

Years	France	Germany	England	Belgium	Spain	Italy	Switzerland	Netherlands
1906	14	5	9	12	47	28	4	
1907	15	4	6	11	41	25	5	
1908	12	5	7	11	34	27	3	6
1909	10	4	6	9	27	28	3	5
1910	8					26	4	
1911						27·5		
1912						22		

Spain, Russia, Italy, France, Belgium and Roumania are among the countries which suffer most from typhoid fever.

The etiological conditions which cause the outbreak of the disease are indeed common to the soldier and

the civilian. The special susceptibility of the soldier certainly helps to explain the remarkable frequency with which he is affected.

The following table shows the respective percentages of cases due to this disease in the principal *armies* in time of peace.

TYPHOID FEVER IN VARIOUS ARMIES

Incidence per 1000 *men*

Armies	1903	1904	1905	1906	1907	Average for the 5 Years
French . . .	5·10	5·30	3·70	4·53	3·74	4·49
German . . .	0·95	0·79	0·77	0·51	0·41	0·68
English . . .	0·80	0·80	0·60	0·60	0·70	0·70
Austrian . . .	1·60	1·60	2·10	2·0	3·10	1·88
Bavarian . . .	0·47	0·22	0·93	0·11	0·17	0·38
Belgian . . .	1·89	3·10	1·35	0·82	0·86	1·60
Spanish . . .	2·60	4·82	3·68	4·72	2·87	3·73
Italian . . .						4·92 [1]
Roumanian . .	4·80	4·08	6·90	5·33	3·57	4·73
Russian . . .	5·30	3·80	5·10	5·60	5·50	5·06
United States .	5·14	4·77	3·39	6·15	3·87	4·66

It is important to note that the incidence and mortality of typhoid fever in the French army are diminishing appreciably and, one may say, every year, thanks to the careful hygienic measures adopted. The institution of antityphoid vaccination began to reduce the incidence of this disease commencing with the year 1913. It is found, however, that in the distribution of cases throughout the country, there is a regular predominance of typhoid fever in the army corps in the south and south-west of France, viz. the XVth at Marseilles, the XVIth at Montpellier, and the XVIIth at Toulouse, as well as among the troops stationed in the west of France, *e. g.* Xth Corps (Rennes), XIth Corps (Nantes).[2]

[1] From 1900–1903 (both inclusive).

[2] In the French army, Algeria and Tunis, by their high incidence of typhoid fever, raise the general percentage incidence.

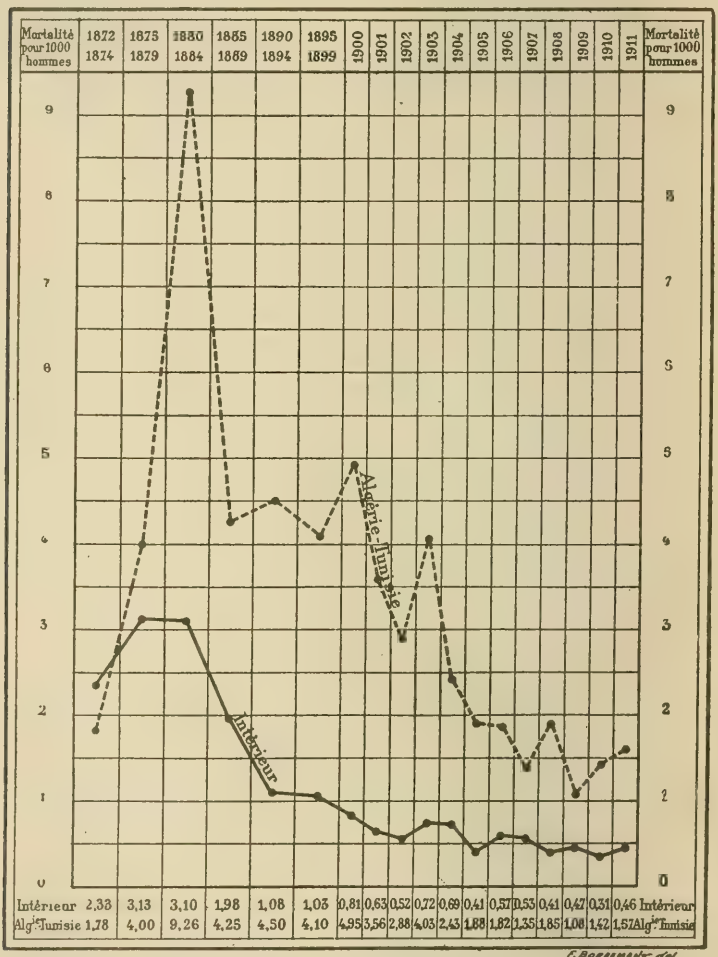
In these same regions the civil population also pays a high toll to the same disease, as Brouardel had observed long ago. Owing to the close parallelism existing between the diseases of the civil population and those of the army, Spain, Roumania, Italy, France,

Russia, the United States, etc., are among the nations whose civil population, like their army, shows the highest typhoid mortality.

Typhoid Fever in War Time

No conditions predispose so much as war to the outbreak of typhoid fever and paratyphoid diseases. Marston,

a Medical Officer of the American army, has rightly called typhoid fever "the greatest scourge of armies in time of war." Thanks, however, to the hygienic



measures adopted, modern wars are far from showing the appalling incidence of the wars of bygone times.

The War of Secession (*June* 1, 1861–*June* 30, 1866) put in the field 431,237 men, who showed 75,368 cases of typhoid fever, or 175 cases per 1000, and 27,056

deaths, or 57·78 deaths per 1000. Out of 1000 deaths due to all causes, 209 were caused by typhoid fever. Even these figures do not include the cases of typho-malarial fever, *i.e.* the association of typhoid fever and malaria.

During the *Franco-German War* of 1870, the German army, whose effectives were 815,000 men, had 73,396 cases (80·3 per 1000), and 6965 deaths due to typhoid fever.

The *Turco-Russian War* of 1877–1878 furnished another proof of the intensity of typhoid infection among troops in the field.

The Russian army of the Danube, comprising 529,000 men, had 25,000 cases of typhoid fever (not including the cases of " undetermined typhoid diseases "), or 42 cases per 1000, with 7800 deaths, or 12 deaths per 1000, whereas this army lost in battle only 4955 men.

The army of the Caucasus, which suffered most, had 24,473 cases, or 99 per 1000, and 8900 deaths, or 36 deaths per 1000, as compared with only 1975 who were killed by the enemy.

We have here an example of the extreme gravity of typhoid fever as well as of its frequency in the combatant soldier. Of 100 typhoid cases, 36 succumbed.

During the campaign in *Bosnia-Herzegovina*, out of 2085 deaths due to various diseases, 944 were caused by typhoid fever.

The *Tunis Expedition* in 1881, and the *South Oran Expedition* in the same year, offered numerous examples of the extreme gravity of typhoid. The army of 20,000 men sent to Tunis had 4200 cases (one case among five men) and 1039 deaths (more than one death in twenty). The Innocenti Column (21,000 men) sent into South Oran had 1400 cases of typhoid fever and 425 deaths.

The small French Column which took part in the Allies' Expedition to China had 633 cases and 100 deaths.

In the *War with Spain* the American troops, con-

sisting of a force of 107,937 men, suffered severely from typhoid fever. The average proportion of cases was 192 per 1000. There were nearly 3000 deaths.

The first division of the first corps, with a force of 11,339 men, during its stay at Chickamauga Camp, and after leaving the Camp, yielded a total of 1921 cases.

The second division of the same corps (11,357 men) had 2172 cases.

The third division, which suffered most, out of a force of 10,329 men, had 2726 cases, a proportion of 263·91 cases per 1000, or more than *one case in every four men*, with a mortality of 16·36 per 1000.

To sum up. The first, second and third divisions of the First Corps, out of a force of 33,025 men, had 6819 men in hospital for typhoid fever, with 471 deaths due to this cause.

In the *Transvaal War* typhoid fever (enteric fever) was far and away the predominant disease in the English army, of which the average strength was 265,000 men.

Out of 22,450 deaths from disease, typhoid fever caused 7991.

The number of men killed by the enemy was hardly greater—8590. During the Siege of Ladysmith the average number of deaths from typhoid fever was sometimes 10 per day.

In the *German Expedition* against the Herreros there were 1277 cases and 140 deaths. In the period 1905–1907, out of a force of 18,116 men there were 3146 cases of typhoid fever (Kutscher).

The *Russo-Japanese War* offers a happy exception to the observations made in other wars.

The explanation of this will be given later. The Russian army had 21,309 cases, and the Japanese army only 5474 cases of typhoid fever. The disease rapidly increased after August 1904, and reached its maximum in November.

We may remark that the collection of statistics given above really includes under the same heading para-

typhoid fever, the nosological isolation of which is of more recent date.

The War of 1914–1916 has furnished a new proof of the great importance of typhoid fever in armies on active service. During the first months of this war, although the season was remarkably favourable for the outbreak of typhoid fever, in spite, also, of the terrible fatigue to which our soldiers were subjected, typhoid fever proved to be extremely rare. This remarkable result must be attributed to the fact that these young troops, who were made up of contingents coming from the interior, Algeria, Tunis and Morocco, were in very great part immunised by vaccination.

Strategic necessities, as well as the losses sustained in the open field and in the trenches, brought, in successive batches, into the war zone large quantities of fresh troops who were composed, especially at first, of men whom it had been impossible to immunise.

The general mortality of the French Army at the front dropped almost at once, and kept at a very low level as soon as rigorous measures were taken.

It cannot be doubted that if typhoid fever has shown itself very fatal in past wars, it would have been destined to play a preponderant rôle in the pathology of present or future wars if prophylactic measures, and especially vaccination, had not been applied energetically, continuously and conscientiously.

CHAPTER VII

ETIOLOGY OF TYPHOID FEVER

Favouring Causes

Typhoid fever is due to a special bacillus which, after penetrating into the organism, is disseminated in the blood and then settles in the lymphoid organs, Peyer's patches, spleen, bone-marrow, liver and gall-bladder, and nervous system. It gives rise to a *toxi-infection*, the symptoms of which have been described in the first part of this work.

This bacillus is therefore the necessary condition for the development of typhoid fever.

Its mere absorption, however, is not always sufficient to enable it to multiply and give rise to the characteristic disease. In large epidemics the members of an affected community do not all contract typhoid fever, though they are all exposed to the same cause of infection. Some have such mild forms of the infection that it passes unnoticed, even by the patient. Others, and they form the largest number, escape the disease.

In like manner the inhabitants of the same town who have drunk the same contaminated water, the soldiers living in the same barracks and exposed to the same risk of contagion, are not all attacked by typhoid fever. What is the explanation of this?

It is well known that many pathogenic agents, in order to grow in a healthy subject, under ordinary conditions, require a certain number of adjuvant circumstances called *favouring causes*.

Repeated observations have illustrated this special

influence of favouring causes in the etiology of tuberculosis, cerebro-spinal meningitis, pneumonia, etc. There are, indeed, few diseases in which these causes play so important a part as in typhoid fever.

Among these causes there are some which may be called extrinsic, *i. e.* independent of the individual, such as the influence of heat, seasons, etc. Others, on the contrary, are inherent in the individual, one of the best known being that of age.

In practice it is necessary to become familiar with these causes, for if we are powerless to escape from some of them, we should be alive to their favouring action and take measures to check the threatening infection by a still more rigorous prophylaxis.

The rôle of *seasons* in the evolution of typhoid fever has long been known. Although it may appear at all seasons of the year, typhoid fever is specially frequent in the warm season and in the autumn.

The observations of Murchison in England, and of Marc d'Espine, Besnier and Kelsch in France, have shown the predominance of typhoid fever in the æstivo-autumnal period. In towns where the disease is endemic, it is almost always in summer that epidemic recrudescences are observed. It goes without saying that there is no absolute rule in this respect. Some epidemics have occurred in winter, like the epidemic at Cherbourg which broke out suddenly on January 25, 1909, or the epidemic at Tours which began in January and February 1914. The epidemic which began in November and December of 1914, during the great war, may also be quoted.

Generally speaking, however, epidemic cases usually occur in the months of July and August, involving a considerable number of the inhabitants of a village or town, and frequently lasting until November.

The army offers every year, in time of peace, a very remarkable example of this epidemic rhythm. The curve of all the cases and most of the deaths are at their lowest level during the winter season. They rise, sometimes suddenly, on the appearance of the warm

season and keep more or less at this level during this period. The influence—an indirect one, it need hardly be said—of the external temperature on the annual course of epidemics is shown by the fact that in Algiers and Tunis, where the hot season occurs earlier, the rise of the epidemic curve takes place a month sooner than in France; it also lasts a month later.

The disease is also much more frequent in that part of the world.

As we have said, the towns in the South (Marseilles, Toulon, Avignon, Castres, Beziers, Narbonne, Montpellier, Toulouse, etc.) are among those in which the civil population, no less than the military, pays the highest toll to typhoid fever.

There is, therefore, an etiological factor which confers a cyclical character on the incidence of typhoid fever, viz. heat. All the countries on the shores of the Mediterranean, as well as hot and sub-tropical countries, are dangerous foci of typhoid fever. The early history of the occupation of Morocco was marked by a very severe typhoid mortality, which involved the colonists and first immigrants.

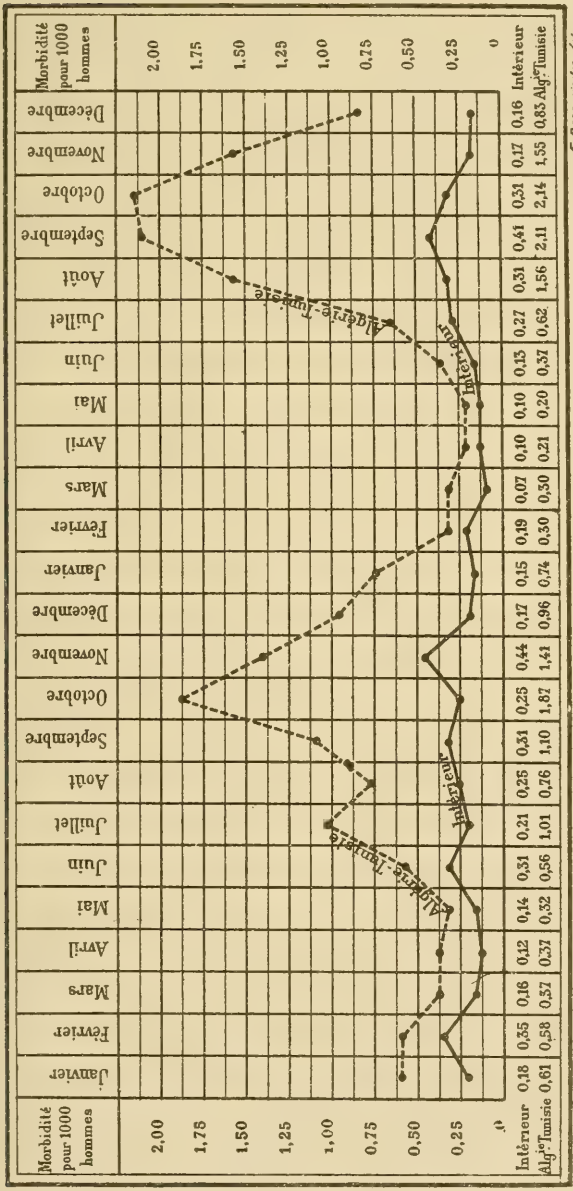
These insanitary conditions, resembling those which marked the occupation of Algeria and Tunis, have to-day been entirely removed—in the army at least.

In the French and Belgian Congo the colonists, manufacturers, explorers, trading companies and companies for developing railways, have supplied typhoid fever with numerous victims.[1]

The disease remains frequent for the same reason in Egypt, India, Eritræa, Central America, the Philippines, etc.

All infectious diseases with an intestinal localisation, such as dysentery, cholera, infantile and ordinary diarrhœa, show an epidemic fastigium which coincides with the high temperature and hot weather.

[1] The influence of heat is shown not only by the number of cases of typhoid fever, but also by their gravity, to which it adds considerably. The severity of the symptoms and percentage mortality are much greater in warm countries.


Morbidité pour 1000 hommes
2,00
1,75
1,50
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1,00
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0
Janvier
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Avril
Mai
Juin
Juillet
Août
Septembre
Octobre
Novembre
Décembre
Janvier
Février
Mars
Avril
Mai
Juin
Juillet
Août
Septembre
Octobre
Novembre
Décembre
Algérie-Tunisie
Intérieur
Intérieur 0,18 0,35 0,16 0,12 0,14 0,31 0,21 0,25 0,31 0,25 0,44 0,17 0,15 0,19 0,07 0,10 0,10 0,13 0,27 0,31 0,41 0,31 0,17 0,16
Alg.-Tunisie 0,61 0,58 0,57 0,37 0,32 0,56 1,01 0,76 1,10 1,87 1,41 0,96 0,74 0,30 0,30 0,21 0,20 0,37 0,62 1,56 2,11 2,14 1,55 0,85 Alg.-Tunisie

In addition to these æstivo-autumnal variations of enteric fever, multi-annual variations have been noted (Besnier), *i.e.* recrudescences of epidemics every five, six or seven years. They are due to the arrival in the same infected locality or town of new and susceptible subjects. The proportion of susceptible individuals is also increased by a certain number of births.

In an estimation of the favouring causes inherent in the man himself, and which act either as a check or as an aggravation of the typhoid infection, much importance must be attributed to the influence of a *previous attack*, as well as to that of age, race and overwork.

The immunity conferred by a previous attack of typhoid fever is very great, but it is not, however, absolute or permanent for a certain number of individuals. It may be calculated that 1 to 2 per cent. of those who have had typhoid fever are liable to contract it a second time. The second attack is usually milder. The interval between the two attacks is from two years (very exceptional) to seven years and more. The second attack of typhoid fever fairly often occurs after a journey abroad, where the subject is contaminated by other strains of the bacillus, as has been seen in colonists or travellers to Morocco. Similar observations have been made in the case of malaria.

There seems to be a familial predisposition for typhoid fever.

It is not uncommon to see an abnormal number of cases of this disease among members of certain families, living under different conditions and in different areas. On the other hand, there is no doubt that certain individuals or races are immune.

As we have seen, typhoid fever is an ubiquitous disease. All races are liable to it. During the War of Secession the coloured troops, though they were less affected than the others, nevertheless had 192·14 cases per 1000 and 57·71 deaths per 1000. In the

Eritræan Campaign the native troops and porters suffered, though in a less proportion, from the same disease.

The Germanic race is as liable to typhoid infection as the Latin. Not only was typhoid fever frequent in the ranks of the German army in 1870–71 and in the present war, but the German prisoners sent to Morocco showed, shortly after their arrival, some epidemic cases, which were immediately checked and arrested by preventive vaccination.

The Japanese race has little susceptibility, as was proved by the rarity of attacks in the Japanese army during the Manchurian War, in which the number of cases was four times less than in the Russian army. The same was found to be the case on the occasion of the Expedition to China in 1901 (Shimosa).

Is this relative immunity the result of previous attacks in childhood among the Japanese, or is it the result of the very rigorous prophylaxis adopted by the Japanese troops? It is impossible to say. The same question, namely, the influence of racial immunity, is suggested by the Arabian and Hindoo races. In spite of very bad hygienic conditions, the Indians rarely suffer from typhoid fever. It is the same with the Herreros. A comparison of the incidence of typhoid fever in Algeria among the Arab troops with that among the French troops living in the same garrison towns has shown that the former had 80 to 100 fewer cases of typhoid fever than the latter (H. Vincent). As a matter of fact, the Arabs in Algeria include men of Aryan race (Kabyles), who are very susceptible. On the other hand, the transfer of Arab soldiers to Morocco has revealed the frequency and gravity of typhoid fever among them. There is, therefore, some reason to think that those who have not been attacked possess an acquired immunity, the result of typhoid fever contracted in childhood, rather than a spontaneous or racial immunity.

A similar reason may be given to explain, on the one hand, the lesser frequency of typhoid fever in

inhabitants of large towns, and, on the other hand, the high susceptibility of country people who have been uprooted and transplanted into towns. The emigration of rural populations into towns exposes them, among other dangers, to attacks of infectious disease, and especially typhoid fever. Servants of both sexes and employees from the country who take up situations in towns in which the sanitary conditions are defective and the drinking water is contaminated, are before long attacked by the typhoid bacillus, especially if they are young. The same observation was made long ago in armies, even during the War of Secession.

Typhoid fever may be observed at all ages. A pregnant woman, when attacked by this disease, may communicate it to her fœtus, as has been shown by numerous examples.

Typhoid fever may also attack old men of eighty years and over. But all epidemiologists have noted the exceptional frequency of the disease during adolescence, and especially in young men or women, single or married. The largest number of cases usually occurs about the twenty-first year.[1] Brouardel, in an analysis of 10,036 deaths from typhoid fever, found that 3896, or *more than a quarter* of the deaths, occurred between the ages of twenty and twenty-five.

J. Bertillon says : " The frequency of typhoid fever is considerable after the second year of life; then it rises until twenty to twenty-five years of age, *when it reaches its maximum.*"

The male sex is much more frequently affected than the female, with the exception of the first years of life.

The increase in the incidence of typhoid fever from twenty to twenty-four years of age specially applies to the male sex : at this age there are fewer cases of

[1] According to Murchison, out of 100 cases of typhoid fever, 46·5 are observed from fifteen to twenty-five years; the average age at which typhoid fever is most frequently contracted is twenty-one years.

typhoid fever in the female sex than between fifteen and nineteen years of age.

From 1876–1905 the average annual mortality from typhoid fever in Paris among 100,000 inhabitants was as follows—

From 0 to 1 year	9·2
„ 1 „ 4 years	50·9
„ 5 „ 9 „	51·3
„ 10 „ 14 „	62·0
„ 15 „ 19 „	95·7
„ 20 „ 24 „	94·0 [1]
„ 25 „ 29 „	53·8
„ 30 „ 34 „	35·0
„ 35 „ 39 „	25·4
„ 40 „ 44 „	17·9
„ 45 „ 49 „	16·7
„ 50 „ 54 „	12·3
„ 55 „ 59 „	10·4
„ 60 „ 64 „	8·7
„ 65 „ 69 „	8·0
„ 70 „ 74 „	5·7
„ 75 „ 79 „	6·0
Over 80 „	7·1

These figures, which have been taken from J. Bertillon's statistics, show that the curve of typhoid fever is fairly low in the first year of life, rises suddenly from one to four years—that is to say, from the time when the child changes his milk diet for one approximating to that of an adult—keeps at about the same level up to fourteen years of age, then shows a new rise, this time a maximal one, between fifteen and twenty-four years. *Young persons of the male sex are most frequently attacked between the ages of twenty and twenty-four.* The frequency of typhoid fever remains high up to thirty, and then progressively falls, a phenomenon which is perhaps explained not only by the diminished susceptibility of advanced life, but also by the immunity resulting from a former attack.

[1] From 1886–1905 the average death-rate at this age was 104·7 per 100,000 inhabitants. The *male sex* had 67·1 deaths, the *female sex* 37·6.

The previous observations, on which Prof. Brouardel often insisted, furnish the explanation of the predilection which typhoid fever has always had for the *army*. Brouardel has dwelt on the principal reason for this. "Statistics," he says, "show that among 10,000 soldiers living in France from 1875–1901 there were 11·2 deaths from typhoid fever, whereas a similar group of 100,000 civilians loses only 3·8." This difference can easily be explained.

"In the population of towns, individuals from fifteen to twenty-five represent almost one-sixth of the total population. Now it is in this sixth part in which is to be found 46·5 per cent. of the cases of typhoid fever, *i.e.* half of the deaths from the disease. This amounts to saying that one-sixth of the civil population furnishes half the deaths from typhoid fever.

"If the civil population is divided by six, and the typhoid deaths by two, and if the proportion per 10,000 inhabitants be worked out, it will be found that the group of fifteen to twenty-five years yields a mortality of 11·5 per 10,000 civilians, while that of the army is 11·2." [1]

For many other reasons, also, a close comparison cannot be made between the morbidity of the civil population of towns and that of the army, which is in great part composed of very susceptible inhabitants from the country. Furthermore, a condition peculiar to the army, without any analogy in the civil population, is constituted by the regular arrival, every three years before the law of March 21, 1905, and every two years since that date, of soldiers who formed part of the army in time of peace. Epidemic diseases are thus supplied with fresh life at frequent intervals, and chances of infection in a military environment are considerably multiplied.

Moreover, in the army soldiers who have only had

[1] This incidence of typhoid fever in the French army has considerably declined. In the years 1909, 1910, 1911, it was 4·7, 3·1 and 4·6 respectively per 10,000.

one year of service always show a higher incidence of typhoid fever than old soldiers.

The same peculiarity has been noted in foreign armies. Thus in the English army in India, in 1899, the soldiers under twenty had 18·8 cases of typhoid fever per 10,000.

The soldiers aged from 20–25 had 31·3 cases per 1000.
„ „ „ „ 25–30 „ 11·5 „ „ „
„ „ „ „ 30–35 „ 5·8 „ „ „

Of all the favouring causes which predispose most to typhoid infection, none is more powerful than *fatigue and overwork*. The influence of these two factors is united in war, especially in those which are violent and prolonged, like the present war.

There is, indeed, no condition which involves such an expenditure of moral and physical energy as war.

Acute overwork may of itself cause death, as is seen in the case of trained animals, such as carrier pigeons. Fatigue and absence of sleep cause a veritable auto-intoxication. The urine and blood, which reveal the saturation of the organism by waste products, are three to four times more toxic than normally. For this reason, after excessive fatigue, and at the moment of recovery, an extraordinary output of urea may be observed (even up to 126 grammes in twenty-four hours, according to Revilliod).

The clinical experiments of Charrin and Roger showed long ago the predisposing rôle of fatigue in infections. The same factor diminishes the principal protective element in the serum, viz. alexine (H. Vincent). It is easy to understand why individuals who have been deprived of part of their means of defence are less successful in resisting infections, and especially such frequent infectious diseases as typhoid and paratyphoid fevers.

Typhoid fever is pre-eminently the disease of the overworked, and, consequently, of war. We have already seen the excessive frequency of this disease. The war in Manchuria was alone an exception to this

law. The favourable sanitary state of the Russian and Japanese armies is explained not only by the hygienic measures adopted by the belligerents, but also because fatigue was almost unknown by the soldiers. The war was characterised by very long intervals of rest, interrupted by a few violent battles.

No condition, therefore, predisposes so strongly to typhoid fever as war, especially war during the æstivo-autumnal season, because the depressing action of heat is added to that of excessive fatigue. During the Tunis Expedition every prolonged march was followed by a recrudescence of typhoid fever.

CHAPTER VIII

ETIOLOGY OF TYPHOID FEVER—THE HUMAN FACTOR—ITS DETERMINING CAUSES

We studied in the last chapter the principal conditions favouring the outbreak of infection due to the typhoid bacillus. By themselves alone they are obviously unable to give rise to the disease.

They arouse the infection, but do not create it.

Further, the disease may quite well develop in a perfectly healthy subject and in the absence of these predisposing factors. It is none the less true that they are often at work either to help on the infection or to exaggerate it.

The typhoid bacillus is the chief cause of the infection. Its most constant portal of entry is the alimentary canal.

After penetrating into the organism by the stomach, the bacillus is or may be rapidly absorbed by the small intestine, especially when it is swallowed in a fasting condition, with impure water, for example, or at the beginning of a meal with such food as oysters.

The very frequent existence of tonsillitis or sore throat at the onset of typhoid fever, which is seen in 40 per cent. of the cases, shows that the tonsils are a fairly common portal of entry for the typhoid bacillus. In some very exceptional cases the ulcerative lesion of the pharynx seems, in association with the fever, to be the only localisation of the infection (pharyngo-typhoid). Although the bacillus has been isolated in the tonsillar exudate (Gallois) these lesions should be regarded as the result of a secondary growth, as is also the case with the spleen (splenomegaly) and Peyer's patches.

The old opinions relating to the modes of infection and penetration of the system by the typhoid bacillus have been modified or rendered more accurate by modern research. It was for a long time believed that the typhoid bacillus grew plentifully in the cavity and walls of the intestine, and thence disseminated the toxins which poisoned the patient. In reality this mode of infection, which is that of bacillary dysentery and cholera, is not applicable to typhoid fever.

The growth of the typhoid bacillus in the intestine is inhibited by the co-existence of bacteria which live there.

Among these hostile micro-organisms the B. coli in particular should be mentioned. This struggle between the saprophytes, which can easily be verified *in vitro*, takes place in the same manner in the digestive tube. Moreover, if a search is made for the typhoid bacillus in the body after death, it is found that the pathogenic microbe *diminishes in frequency towards the lower end of the intestine.*

In reality, the typhoid bacillus after being absorbed by the digestive tract finds a secondary habitat in the viscera, after having first passed through the blood.

This septicæmic period appears to be a silent one.

As the result of systematic cultures of the blood the typhoid bacillus has been isolated during the incubation period, and in the absence of any symptoms, several days before the appearance of the prodromes of the disease. It has also been found in the blood of some healthy subjects who have been contaminated, but nevertheless escape typhoid fever (J. Louis), doubtless because they possess a certain degree of immunity.

From the blood the typhoid bacillus is carried into all the organs and also into the central nervous system. It settles by choice in Peyer's patches, corresponding mesenteric glands, spleen, bone-marrow, liver and gall-bladder.

The presence of the typhoid bacillus in the patient's blood was noted a very long time ago, during life, by

J. Teissier, Busquet, Castellani, Warfeld, Courmont, Lemierre, etc., and after death by H. Vincent.

As soon as the febrile symptoms appear, the bacillus is almost constantly present in the blood. Coleman and Huxon, in the examination of eighty-five cases, found it

during the first week in 93 per cent.
,, ,, second ,, 76 ,,
,, ,, third ,, 56 ,,

It may also be found by cultures for a period of one to four days in the blood of animals infected experimentally.

The early appearance of the typhoid bacillus in the blood thus shows that the specific enteritis, *i. e.* the period of diarrhœa with necrosis of Peyer's patches and intestinal hæmorrhage *is preceded by a very important stage of bacillæmia.*

It is necessary to bear this explanation in mind if one wishes to understand the means by which the typhoid bacillus can be eliminated and thus spread the contagion.

After having invaded the blood, the bacillus is carried by it to all the viscera. From the epidemiological standpoint *this is a fact of great importance, for some of these viscera have excretory ducts or organs which communicate with the exterior,* e. g. the liver by means of the gall bladder and common bile duct, and the kidneys by the ureters and bladder.

From the onset of the disease, and indeed even *from one to twenty-five days* (in cases with a long incubation) *before the appearance of febrile symptoms, the typhoid patient is contagious,* and eliminates the pathogenic bacillus in his excreta.

It is unlikely, at least at this initial period, that these bacilli come exclusively from the mucous membrane and glands of the intestine.

On the other hand, from the moment that the bacillus invades the blood, *the liver and gall bladder form the principal route for elimination of the bacillus of typhoid fever.* The bacillus is also to be found in great numbers

in the stools, to which it communicates their contagious character.

The conveyance of the bacillus to the gall bladder in which it grows is effected, not by the ascending route, *i. e.* from the intestine to the gall-bladder by means of the common bile duct, but by the liver, or, according to Chiarolanza, by the blood capillaries of the submucosa, where they perhaps form emboli, which facilitate their passage into the gall-bladder.

Lemierre and Abrami hold that damage to the hepatic parenchyma allows the passage of the bacillus into the bile.

Whatever may be the means by which it is conveyed, the almost constant presence of the bacillus in the bile remains a well-proved fact.

It may be absent, but this is a rare occurrence. When it reaches the gall-bladder it grows there as readily as in a culture-tube, finding a suitable medium which is constantly being renewed and eliminated, and thereby carries the bacillus with it into the duodenum and discharges it with the excreta.

An attempt has been made by means of experiments to elucidate the problem, which is so interesting from a pathogenic and epidemiological point of view, of the existence of the typhoid bacillus in the gall-bladder. As a matter of fact, animals form an unsuitable field for inquiry, because, with the exception of the monkey, they present a very low susceptibility for typhoid infection. Though very sensitive as regards the toxine, it is only under very rare and special circumstances that they show symptoms of true septicæmia.

Investigators, however, have succeeded in injecting the typhoid bacillus into the vein of a rabbit, and finding it in the gall-bladder when the animals were killed at different dates. Thus the bacillus has been found to persist in the bile of a rabbit for three and even four months. This long persistence of the bacillus in an animal is doubtful, and the same experiments have by no means given a similar result in the hands of other writers.

In man the existence of the typhoid bacillus in the

contents of the gall-bladder may be found by cultures after death. In the patient, Boldyreff's test, *i. e.* the injection of 200 grammes of oil, causes a reflux of bile into the stomach, from which the bacillus can be isolated. It has been possible to find the micro-organism by this method, even when examination of the stools had been negative. Lastly, Carnot and Weill-Hallé have introduced a very interesting method by which the typhoid bacillus can be sought for and isolated in the duodenum by means of a rubber tube.

An explanation is thus obtained of the presence of the typhoid bacillus in a patient's stools. The chief sources from which the bacillus comes are: (1) Infected bile; (2) Intestinal ulceration; (3) Extravasation from the capillaries of the intestinal submucosa (Chiarolanza).

This elimination, which is so important from an epidemiological standpoint, can be verified by cultivation of the stools.

The date of appearance of the typhoid bacillus in the stools is very early, its presence having been observed before the febrile period and even before the first symptoms.

We may remind the reader that typhoid fever is preceded by an incubation period which may be as short as fourteen or fifteen days, but which may be prolonged to three or four weeks, or even forty or forty-five days. The result is that the subject who is incubating typhoid fever may have been disseminating the pathogenic bacillus by direct or indirect contagion for a long time without there being any signs to reveal it.

As soon as the symptoms of the disease appear, and the typhoid diarrhœa sets in, there is an abundant elimination of the bacillus, especially during the attacks of diarrhœa. In cases in which the biliary secretion is increased the intestinal content is rapidly eliminated and is very rich in bacilli.

The liquid character of the fæces facilitates their dispersion, and consequently the likelihood of contagion among those who are looking after the patient.

The excretion of bacilli is most copious during the

first fortnight, and then diminishes. Some writers think that the maximum frequency of the bacilli in the stools occurs at the onset of convalescence (?). It is women especially who have been weakened by a protracted attack of typhoid fever who eliminate most bacilli.

We may conclude from the foregoing that the patient excretes the bacillus and that consequently he is contagious before the appearance of the febrile symptoms and throughout the duration of his infection.

In hospitals patients suffering from characteristic forms of typhoid fever are usually isolated and are subject to precautions which remove or restrict the dangers of contagion. But in families, especially in poor families or in the country, the contagion may spread with extraordinary facility.

Hence those epidemics in families or villages in which a large proportion of the members or inhabitants are successively attacked. Individuals who have mild forms of the infection which are known as abortive, attenuated (*typhus levissimus*) or ambulatory, constitute some of the most dangerous agents of contagion because they are unrecognised. Such patients may be walking about and even be engaged in their ordinary occupations for several weeks, while they are disseminating the bacilli in their excretions, contaminating their neighbours and sometimes creating fresh foci of infection at a distance.

Children often serve as unrecognised agents in the dissemination of the typhoid bacillus by means of their excreta. Contrary to the generally accepted view they are very susceptible to this disease. Usually, however, they have only slight attacks accompanied by a weak febrile reaction, but on the other hand by diarrhœa, which may be profuse.

The *stools* of patients suffering from typhoid fever consequently form *the most important means of contagion* on account of the bacillus which they contain.

There are other means of contagion which we will now discuss.

It is well known that typhoid patients in the course of their disease fairly often have albuminuria and bacilluria. Although these two phenomena are not invariably associated, they may accompany each other. The discharge of typhoid bacilli in the patient's urine was described long ago by various writers (Neumann, Petruschky, Richardson, Wright and Semple, etc.). As in the case of the fæces, though in a less degree, the isolation of the typhoid bacillus in the urine presents difficulties. This is particularly the case when *B. coli* is also present. The presence of the typhoid bacillus in the urine of patients varies. Wright and Semple found it in five out of six patients.

Other authors isolated it in only 19 per cent. (H. Vincent). As in the case of the gall-bladder the bacillus may multiply in the bladder and cause an inflammation of its walls and even hæmorrhagic cystitis.

Cases of hæmorrhagic nephritis due to the growth of the bacillus in the renal parenchyma may also be observed in the course of typhoid fever.

In these various cases *the urine becomes a factor of contagion which is by no means negligible.*

The appearance of the typhoid bacillus in the urine in typhoid fever is not so early as in the biliary secretion. Whereas the bile forms a favourable culture medium for this bacillus—a property taken advantage of for the isolation and cultivation of typhoid bacilli (and paratyphoid bacilli)—the same cannot be said of the urine, which is an acid and innutritious medium.

It is none the less true that the passage of the typhoid bacillus into the patients' urine may play a part in the transmission of the disease.

It will be seen later that the typhoid bacillus may persist sometimes for a very long period after recovery in the gall-bladder, and consequently in the stools, as well as in the bladder and urine.

There are a certain number of atypical forms of infection due to the typhoid bacillus, which undoubtedly have a share in the transmission of typhoid fever. Such are the cases of septicæmia without intestinal

lesions, of which examples have been published, and certain forms of appendicitis (Drigalski, Stokes and Amick), suppurative otitis, bronchitis with obstinate bronchorrhæa without signs of typhoid fever, etc. Netter has observed instances of vulvitis due to the same infection in little girls.

More closely associated with typhoid fever are the late typhoid infections of the gall bladder and bile ducts, which very often occur in an apparently spontaneous manner and independently of any previous attack of typhoid fever. The typhoid bacillus has none the less penetrated into the organism at some time or other, sometimes without causing any immediate reaction, sometimes giving rise to a slight and overlooked affection, but in any case after a phase of latent septicæmia.

The importance of these foci of contagion from an etiological and hygienic point of view cannot be denied. By isolating the typhoid bacillus from the bile, after operations and at autopsies on patients suffering from hepatic colic, acute or chronic angiocholitis, cholecystitis and jaundice, Dupré, Dauriac, and Gilbert and Fournier made a highly valuable contribution to medical science, whereby this class of patients may be classified as *germ carriers*. The bacillus has been isolated from gall stones.

Paratyphoid bacilli also may be responsible for the same lesions. A certain number of cases of surgical contagion shows that this factor is not an exception (Ribadeau-Dumas and Debré). Wherever the typhoid bacillus can grow, and in whatsoever condition it may multiply, such as cholecystitis, suppuration, abscesses, osteitis, or periostitis, thyroiditis, parotitis, etc., it is liable to be contagious.

But transmission of contagion in this manner is much less frequent than by the fæces or urine.

It is not unreasonable to suppose that the typhoid bacillus may exist in other pathological products, or be propagated by other natural secretions. It may occur in the blood from epistaxis or intestinal hæmorrhage.

The pharyngeal lesions occurring at the onset or in the course of typhoid fever, such as Duguet's ulcers, may explain the presence of the bacillus in the saliva in which Dvouyeglasoff and Chantemesse have found it, the former in two out of fifteen cases, on the twelfth and twenty-fifth days of disease. Manicatide, who took cultures from the pharyngeal and tonsillar secretions of fifty-one patients, isolated the bacillus in thirty-six cases. Gallois has insisted on the importance of the rhino-pharyngitis, which is a fairly frequent prelude to typhoid fever. Systematic cultivation of the saliva, however, by other writers, did not show the bacillus.

Do the bronchial secretions of patients with pulmonary complications contain the bacillus?

Jehle says that he found it in nine out of fifteen cases after death. We have already alluded to the fact that certain forms of bronchitis, with abundant expectoration, are rich in bacilli.

As a matter of fact, pulmonary complications occurring in typhoid fever are due to secondary infections of the parenchyma or bronchi. Bacteriological examination shows the staphylococcus or streptococcus, which are the real cause of these infections, and in cases of pneumonia the pneumococcus alone (H. Vincent). The typhoid bacillus is found in the lung, but not as a rule in the spitting-cup. If, however, the lesion is accompanied by ulceration or hæmorrhage, the typhoid bacillus may be entangled in the pus or blood, and thus become an exceptional agent of contagion.

The same remark applies to the healthy and damaged skin (bed sores), and the sweat, in which Sudakoff and Wigura isolated the bacillus.

But contamination by fæces and bath water are sufficient to explain its presence on the surface of the skin.

In the case of two nursing women suffering from typhoid fever, Chantemesse and Widal were unable to discover the bacillus in the milk, but Lawrence says that he isolated it in one case of the kind.

Bilious vomit may contain the bacilli in very large

numbers. This vomiting, which occurs at the onset of typhoid fever, is connected with the infection of the bile passages. The reflux of bile into the stomach and its hyper-secretion brings with it a number of contagious bacilli.

We may conclude from the foregoing that the typhoid bacillus is eliminated by the patient before any symptoms appear, and throughout the duration of the disease.

The contagiosity of patients suffering from typhoid fever is consequently due to the presence of the typhoid bacillus in the excreta, urine and vomit, and in an accessory degree in the other secretions, including pus and other pathological products. The patients' dejecta constitute the most dangerous elements in the transmission of the disease.

The corpses of persons who have died of typhoid fever are, for an indefinite period, it is true, sources of infection of the soil and subsoil water, to which they contribute an enormous quantity of germs. But it must be stated that this mode of infection is limited owing to the feeble vitality of the typhoid bacillus outside its natural culture medium, the human body. On the other hand, we do not know of any animals which spontaneously contract typhoid fever, which is, therefore, a pre-eminently human disease. Moreover, in the presence of the micro-organisms of putrefaction and those of the soil, the typhoid bacillus does not survive for long. It dies as the result of a struggle for life with the other bacteria. It is, indeed, a general law that most pathogenic microbes, and especially the micro-organisms, which are pathogenic for man exclusively, cannot multiply outside the human body. Some survive in this external medium for a comparatively short time, but all die and sometimes very rapidly.

The result of this is that the contagion of infectious diseases demands for its realisation an assemblage of conditions which can easily be determined, in the majority of cases, when the pathogenic agent can be

cultivated and isolated by laboratory methods. Such is the case in typhoid fever. This possibility of determining the presence of its pathological micro-organisms has enabled us to study in detail another important factor in its transmission, the "germ carrier."

CHAPTER IX

ETIOLOGY OF TYPHOID FEVER (*continued*)—THE HUMAN FACTOR—THE RÔLE OF CARRIERS

THE bacteriological researches which have been made by a large number of investigators have clearly proved the effective survival of the typhoid bacillus in the patient, in spite of his recovery from the disease. It has already been shown that some cases of periostitis or osteitis occurring sometimes even several years after recovery from typhoid fever might contain the living bacillus. On the other hand, a long time ago a certain number of French physicians established the relation existing between acute or chronic biliary infections, cholecystitis or cholelithiasis and the typhoid bacillus which they had isolated by cultures (Dupré, Langlois, Gilbert and Fournier, Faitout and Ramond, Sacquépée, Carnot, etc.).

Epidemiological observations and the undoubted transmission of typhoid fever by healthy subjects who had had the disease a long time ago, led to an inquiry as to the explanation of this method of contagion.

The subject who has recovered from typhoid fever, or from one of the atypical forms of this infection, the individual who had been merely touched, as it were, by the bacillus, but had nevertheless given it a shelter, however brief it might be, in his blood, gall-bladder, renal pelvis or bladder, is not always freed from the infective agent by the mere fact of his recovery.

In a fairly large number of cases the bacillus may survive the disease. *Clinical recovery does not mean bacteriological recovery.* And thus we find the explanation of the abnormal prolongation of certain epidemics,

of "typhoid fever houses," of cases of contagion hitherto unexplained, and apparently spontaneous cases. All are due, or may be due, to the conveyance of the typhoid bacillus by *bacillus carriers.*

We must now make a study of those healthy subjects who are unconsciously carrying the pathogenic organism, disseminating it about them and are thus becoming dangerous agents of its transmission.

When the fæces of persons recently recovered from typhoid fever are grown on an appropriate medium, colonies of the typhoid bacillus may be found in some of the specimens.

Further examinations show, though not invariably, the persistence of the bacillus in their excreta. Such persons are germ carriers.

The first researches on germ carriers were made by Remlinger and Schneider in 1897 at the Val-de-Grace School. On examination of the fæces of ten soldiers who had been treated for various affections, these observers isolated the typhoid bacillus in five cases.

In a publication which appeared shortly afterwards Prof. Lemoine, of the same school, also found the bacillus in the fæces of a certain number of patients who were not suffering from typhoid fever, tuberculous patients in particular. One of us also isolated the bacillus from the excreta of a healthy subject in 1893.

In 1904 Clerc and Ferrari found the bacillus in six out of thirty-two persons who were in charge of typhoid patients.

It was not till several years afterwards that these researches were universally confirmed and demonstrated the existence of the bacillus in a fairly high number of "carriers."

In 1903 Decobert also drew attention to the existence of convalescents from typhoid fever who showed the bacilli in their fæces. He found the typhoid bacillus for fifteen to twenty days, and in one case for more than a month after the temperature had become normal.

Braun found one patient in twenty, and Sicre one in ten, who still showed the bacillus in the fæces after

recovery from typhoid fever. Sacquépée found two chronic carriers among eleven patients, etc.

The origin of the typhoid bacillus which has been thus eliminated in the fæces is in the gall bladder.

In this cavity, where the bacillus finds a nutritive medium in which it can grow, the microbe lives and multiplies and can be found long after recovery, just as, in the course of the disease, in the dejecta. The proportion of bacilli contained in the stools of germ carriers may be considerable. Researches made at the laboratory of the *Army Medical Advisory Board* show that carriers can eliminate daily from 30–190 millions of bacilli per gramme of excreta.

The excreta of the carrier thus become the efficient cause of typhoid fever on every occasion on which they come in contact, directly or indirectly, with the healthy subject. This is the explanation of some persistent endemics, especially in villages, families, camps, and cantonments and trenches in war time, in spite of an early removal of the sick, the disinfection of excreta and soiled linen, and the sterilisation of drinking-water.

The bacillus is also conveyed by persons suffering from ambulatory, abortive or atypical forms of typhoid fever in which no precautions are taken. It is no less certain that men in the incubation stage or at the onset of typhoid fever are very dangerous propagators of the bacillus, especially in war time, when soldiers frequently refuse to consult the doctor from a variety of motives, whether through fear of having their suspicions as to the nature of their disease confirmed, or because war has accustomed them to neglect their physical sufferings, or because they are too proud to seek advice. Some men do not report themselves sick until their strength entirely gives way. It is thus that we find cases of acute peritonitis, or of sudden death from myocarditis in patients suffering from typhoid fever.

Convalescents and persons who have recovered from the attack many years previously act as carriers of the typhoid bacillus.

Their rôle in the propagation of the disease is not exclusive. It is not, however, a negligible one, and in circumstances which we shall discuss later it is predominant.

There are two groups of bacillus carriers: *the biliary* or *fæcal* carrier, and the *urinary* carrier. The growth and persistence of the bacillus in the urine are due to the same causes as the survival of the typhoid bacillus in the bile.

German hygienists have made a distinction between "primary" germ carriers, *i. e.* those who had never been ill, and "secondary" carriers, *i. e.* those who had previously had typhoid fever. This distinction has no practical interest and, further, by the suggestion that the bacillus has escaped from the body without having caused a previous infection of the blood, however short-lived and slight it may have been, is not in conformity with facts. In carriers who have never had typhoid fever there is always a period of blood infection which precedes the growth in the gall bladder.

As we have seen, in epidemic times individuals are to be found who have the bacillus in their blood, although they are free from typhoid fever. Further, the serum test is positive in a certain number of healthy individuals, which also proves in another manner the reality of the infection.

We will now discuss *temporary* carriers and *chronic* carriers.

The duration of the persistence of the typhoid bacillus in the stools of germ carriers varies considerably. It ranges from a few weeks to months or years. It may even continue throughout life.

After recovery from typhoid fever the bacillus either disappears from the stools—the most frequent event—or it may still persist in them. The proportion of those in whom it persists is from 4 to 5 per cent. Park estimates this number at 6 per cent. Of these a third (2 per cent.) keep the bacillus for several weeks or two to three months. About 1 per cent. remains a carrier from three months to a year. Beyond this date the

number of chronic carriers is a little more than 1 per cent.

The statistics obtained by examination of the stools vary with the observers. Cases in which the bacillus may be found in the excreta for ten, twenty or thirty years, and even longer, are doubtless less numerous, but are by no means exceptional.

The predominance of typhoid carriers in the female sex is a well proved but unexplained fact. The difference between the two sexes is considerable. On the other hand, the number of carriers among children is much less than among adults. Children aged eighteen months have been found to be carriers.

If chronic carriers only be considered, 79 per cent. are women and 21 per cent. men.

A similar examination made among children showed that 4 per cent. were chronic carriers.

Frequent cultivation of the stools of carriers fairly often shows that there are periods during which no elimination takes place.

This disappearance of the bacilli occurs very irregularly. Absence of bacilli may be noted at the *onset* of convalescence, and their presence several months afterwards.

Subsequently the presence of the typhoid bacilli in the fæces is also sometimes continuous and sometimes intermittent.

Intervals of varying length occur which may last one or more weeks and even two or three months, followed by a return or even a considerable increase in the number of bacilli eliminated. It is obvious that germ carriers are dangerous during these periods of activity. D. S. Davies and Walker Hall have even thought that their period of contagiosity was related to the seasons (from May to November in England), but this view has not been confirmed.

It is therefore necessary for the detection of carriers to have recourse to repeated examinations for a fairly long period, *e. g.* six months to a year at least.

This, it must be admitted, is a method of difficult

application in a large community, especially when one considers that the isolation of the typhoid bacillus from the stools requires some experience owing to the frequent presence of bacilli of the paracoli group and *B. fœcalis alkaligenes*, which grow abundantly in the intestine, and on superficial examination may be classed as typhoid bacilli. The agglutination test has, therefore, been recommended, as it is positive in a 1 in 100 dilution among three-quarters of the carriers.

Carriers chiefly consist of persons who have recovered from the disease some time previously. But it has been said that persons who have never had typhoid fever may also harbour the bacillus. Their attack has been mild or unrecognised and left this latent condition as a residue.

It has been noticed that such carriers are chiefly found among persons who have been near typhoid patients, such as nurses, male or female attendants, doctors, and generally any persons who have been attending them.

Sometimes carriers themselves have been known to contract typhoid fever.

The duration of the persistence of the typhoid bacillus in the gall-bladder varies considerably. Although, as a rule, its persistence does not exceed three months, a certain number of carriers remain infected and infectious for ten or twenty years and even more. Some keep and discharge the bacilli throughout life. Donald Gregg reported in 1908 the case of a woman who had had typhoid fever in 1856, but had been in good health since, except for attacks of migraine accompanied by diarrhœa, and who still had the typhoid bacillus in her stools after fifty-two years.

These temporary or chronic carriers thus become the starting-point of isolated or epidemic cases, either in their home surroundings or in places in which they may have stayed for only a short time. They may transmit the bacillus by direct contagion or by agents of various kinds.

Carriers, therefore, play an important part in the

propagation of typhoid fever. The modes of contagion are obviously similar to those which are due to actual patients who are, properly speaking, carriers. There is, however, an important distinction between the two. Patients being isolated and compelled to stay in bed cannot by themselves spread the disease. They may directly infect those who come near them, but the conveyance of the germ to the outside world depends upon the fate of the excreta in which it is mixed. Every object which has served for the personal use of the patient thus becomes an actual vehicle for the bacillus (bed linen, basins, etc.). The germ carrier, on the other hand, is not deprived of movement by disease, but goes from place to place, and may take the bacilli wherever he deposits his excreta. Patients are under close observation, their condition attracts attention and involves special precautions and measures of disinfection, whereas germ carriers escape recognition.

It may be mentioned that the typhoid carrier does not, as a rule, excrete so large a number of bacilli as the typhoid patient, except during periods of diarrhœa, in which the amount is considerable. Some carriers, however, have unintermittently an enormous quantity of bacilli in their stools and in almost pure culture.

It has been urged that the bacilli discharged by germ carriers are less virulent and less active than those eliminated by the patients. This hypothesis is not verified by facts. Numerous family epidemics which have been caused by the direct contagion of germ carriers have given rise to fatal cases.

The foregoing remarks apply also to urinary carriers.

The persistence of bacilluria after recovery from typhoid fever is from a few weeks to several months or several years (Youdalewitch, Wright and Semple, Richardson, H. Vincent). Contagion by urinary germ carriers, however, is less frequent and important than by carriers of biliary origin.

Instances of contagion due to both have been quoted in every country.

It has been observed that epidemics or endemics recur, sometimes every year, in the immediate neighbourhood of germ carriers.

Among the histories of epidemics published, one of the best known is that observed in 1907 by Dr. Soper, Medical Officer of Health for the City of Boston. A cook who had had typhoid fever in 1900 gave rise to thirty-eight cases of typhoid fever in the various families in which she had successively been employed since her recovery.

D. Gregg's case, who had had typhoid fever in 1856, gave rise to seven cases of the same disease in her immediate surroundings between 1905 and 1908, or fifty-two years after her infection.

Huggenberg has recorded the case of a woman in Central Switzerland who had had typhoid fever thirty-one years before and still presented bacilluria. She had transmitted typhoid fever to her husband in 1886, to her son in 1892, to four servants from 1899 to 1902, to her daughter-in-law shortly after coming to live with her, and in 1903 to 1905 to four other servants. In 1908 a fresh case of contagion was found in a servant. No case occurred in her immediate surroundings between 1905 and 1908, but at that date her servants were already infected.

W. Park, Director of the New York Department of Health, has published a very similar case to that of Soper.

The case was that of a cook, who declared that she had never had typhoid fever. She nevertheless caused an outbreak of typhoid fever in seven of the eight different families in which she was successively employed. The total number of cases to which she thus gave rise was as high as twenty-eight.

Her blood agglutinated the typhoid bacillus, which was also found in the excreta. She had to be isolated in the North Brothers Island Hospital.

In the Report on Epidemics to the French Home Office, H. Vincent (Académie de Médecine, 1909) recorded some cases of contagion due to carriers, sick

and otherwise. Direct contagion from man to man is the rule in the country.

At Castelfranc, a village of 463 inhabitants, in the Lot Department, a girl aged ten, who had come from another village in which there was an epidemic caused by the water, infected six living in her house or neighbouring houses.

In Cévan a young child, who had been infected in another village by her nurse, gave rise to six cases. The child of the new nurse, three brothers and sisters, the nurse's mother and servant were infected in succession.

Courtois-Suffit and Beaufumé have published the account of an epidemic transmitted by a germ carrier. After her arrival in a village in the Yonne Department she gave the disease to fourteen persons in her family or in the neighbouring houses.

Numerous descriptions have been published of epidemics due to germ carrriers in schools, seminaries and lunatic asylums. The army is not exempt. Netter recorded the outbreak of twenty-one cases which occurred without obvious reasons in one out of three batteries in a garrison in the East of France.

The food and water supply were common to the three batteries, moreover the drinking water was sterilised. But the infected battery contained a young soldier who had had typhoid fever seven years previously and whose stools contained numerous bacilli.

The same author has also given an account of an epidemic on board a Japanese man-of-war, due to two carriers. When these had been isolated, the epidemic disappeared.

In 1908 a certain number of cases of typhoid fever having occurred at Aldershot Camp, without obvious cause, all the men were examined. One of them had bacilli in the urine. He had contracted typhoid fever in Aden in 1904. He was isolated and the epidemic ceased.

In August 1901 a young soldier, who had typhoid fever three months previously, arrived in England

from South Africa. A fortnight later three sisters and two brothers of the patient, a young servant, the cook, a friend and two persons living in the next house were attacked in succession. The young soldier's urine contained 175 bacilli per c.c. The infection had occurred as the result of the well water, which communicated with the water closet.

The attention of English doctors in India has been directed to typhoid bacillus carriers.

Typhoid fever was very frequent among the troops, since prior to the adoption of preventive inoculation there were at least 1000 cases yearly (not including the much rarer cases of paratyphoid fevers A and B), with the result that every year germ carriers were left to carry on the disease.

For this reason ever since 1908 convalescents from typhoid fever are sent to the special depot at Naini-Tal, which is isolated and provided with a disinfecting apparatus and a laboratory. The urine and fæces are examined there every week, and patients who have recovered from typhoid fever are kept here for four months.

Most of the men keep the bacilli in their stools for a few weeks only. Chronic carriers, *i. e.* those who keep the bacillus for six months, are discharged from the service. Their proportion has been 3 per cent. After the first year (1908) a drop of 9 per cent. was observed in the incidence of typhoid fever among the units in which these precautions had been taken, while the others showed an increase of 26 per cent.

In a new Parliamentary Report (December 25, 1909) it was noted that the duration of the persistence of the bacillus necessitating discharge from the service had been lowered to three months. At the end of this time the man is discharged, unless he prefers to remain in hospital. The Medical Officer of Health for the district to which he goes on discharge from the service is notified of the case. It is to be feared that these carriers on return to civil life may become the starting-point of an epidemic.

Questions were raised in the House of Commons on the subject of soldier carriers who had been sent home from India and isolated at Millbank Military Hospital.

Public authorities have everywhere been much concerned about the danger likely to result from these carriers, owing to the absence of help hitherto afforded by prophylaxis. In France this problem has been studied by the Health Service of the army, and gave rise in 1910 to an important discussion at the Academy of Medicine. In England, Germany, Russia, Belgium, and the United States, especially at the State Board of Health of Iowa, sanitary legislation has endeavoured to find a remedy for the conveyance and propagation of typhoid fever by these carriers, but this special prophylaxis meets with very great difficulties, as may well be understood.

Families and persons living in immediate contact with the carrier are most exposed to the risk of contagion. Life in common leads, indeed, sooner or later, to direct or indirect conveyance of the bacillus to other persons.

It is, therefore, in poor families, in working-class households, or in the country that contagion due to carriers has most chance of developing.

In the army the rôle of typhoid (or paratyphoid) carriers in time of peace is certainly limited to a few special cases. But it becomes considerably more important in camps, and especially in war time, when the crowding together of a considerable number of effectives results in the soil being saturated with human excreta.

The chances of infection are thereby extraordinarily multiplied, especially when associated with even more important factors, such as the presence of those who are really suffering from the disease, both those who are under treatment, and still more so those who are not, *e. g.* soldiers in the incubation period and at the onset of typhoid fever, as well as those who have only an incomplete form of the disease. We have

thus an explanation of the disastrous intensity of the epidemics by which armies were formerly ravaged during even the shortest wars.

We have now to discuss those circumstances that favour epidemic contagion. After having studied the sources *from which* the typhoid bacillus *comes*, we must state *whither it goes*.

CHAPTER X

THE PRINCIPAL MODES OF DIRECT TRANSMISSION OF THE TYPHOID BACILLUS

After leaving the patient or the carrier, *the pathogenic bacillus of typhoid fever follows the path of the excreta and pathological products in which it is incorporated.* When it comes in contact with a susceptible person the micro-organism can exercise its infective power either in the immediate surroundings of the patient or carrier, or at a distance from its original focus.

The bacillus makes its way into the system either by direct or indirect contagion. The digestive tract is almost always the portal of entry. How does the infective agent gain admission?

The simplest mode of transmission is by direct contagion. Whether eliminated by a patient or a carrier, the micro-organism is, as a rule, communicated without any intermediary agent to persons in their immediate surroundings, such as relations, doctors, nurses, visitors, patients in the next bed, etc.

This direct contagiosity of typhoid fever was well known to the old observers, such as Louis, Gendron and Piedvache. On meeting with successive cases in the same family which were undoubtedly connected with one another, Louis, at the beginning of the nineteenth century, declared that typhoid fever was certainly contagious, at least in the country. Insufficient hygienic precautions, absence of cleanliness, the non-disinfection of excreta, and soiled linen furnish an explanation of this transmission of the micro-organism.

Direct contagion most frequently takes place when the patient is being attended to in connection with defæcation or micturition, the change of body linen or bedclothes, or when he is being carried to the bath.

It may also occur when he is given a drink, or his mouth and teeth are being cleansed, or a visitor shakes his hand which has been contaminated. Contagion occurring in hospitals, as a rule, is due to these factors. Numerous cases are recorded in which patients have been infected by offering their services to a typhoid patient in the next bed.

The carrier may directly transmit the germ in the same manner whenever he is suffering from a disease which requires similar attention, whatever its nature may happen to be. Likewise the patient who is suffering from suppuration due to the typhoid bacillus, or has been operated on for typhoid cholecystitis, etc., may transmit the disease to an attendant who does not take proper precautions.

On the other hand, the contagion may be conveyed by a male or female attendant, who is a carrier, to children or adults suffering from another infection. Uncleanliness is, indeed, almost always at the root of direct contagion. Furthermore, whatever the means by which the contagion takes place, *the hands are, after all, the receptive organs and transmitting agents of the typhoid bacillus.* The hands are contaminated by the particles of fæces, drops of the patient's urine, vomit, sputa, etc., and *without being washed* collect and convey the food to the mouth. For this reason it has been rightly said that, whatever may be the origin of the bacillus, whether from a patient or a carrier, *typhoid fever by contact is a disease caused by unclean hands* (H. Vincent). This statement is further confirmed by the fact that it is the carrier's unclean hand which manipulates the food, contaminates it with bacilli, and so passes it on to other persons about him.

The denomination of "epidemic by contact" has been given in Germany to those cases of typhoid fever which occur in the immediate neighbourhood of the

patient or carrier. This expression is incorrect, for it includes at once direct and indirect contagion. It should be reserved for those cases in which the conveyance of the bacillus takes place directly by contact of the patient with a healthy subject.

From this point of view direct contagion occurs in barracks only under exceptional circumstances, having regard to the other and undoubtedly more numerous risks of infection to which the soldier is exposed in peace time.

The danger of the germ carrier mainly depends on the mode of life of the carrier himself and of those with whom he lives. Investigations made at thermal stations like Vichy, which are the resort of patients suffering from chronic hepatic affections and of active germ-carriers, have undoubtedly proved the extreme rarity of contaminations due to carriers. The fact is that the spread of the contagion of typhoid fever among neighbours is by no means comparable to that of some other diseases, such as diphtheria, cerebro-spinal meningitis, the eruptive fevers, mumps, etc. Whereas in the latter infections direct contagion plays the principal, preponderating, and even, in some diseases, exclusive part, the same cannot be said of typhoid fever.

In the carrier the typhoid bacillus, instead of being in direct and immediate contact with the outer air, is hidden in the gall-bladder and intestine, or in the bladder. It is eliminated intermittently and mixed with the fæces or urine. The result is that the conditions are less suitable for its reaching the outer world and for directly infecting the persons in the immediate vicinity. Such infection could only occur if the bacillus had its habitat in the carrier's saliva or nasal or pharyngeal mucus, which is not the case.

Consequently, direct contagion by the typhoid bacillus is restricted to well-defined conditions. It can only occur when particles of fæces or urine, conveyed by unclean hands or by bedpans or urine-bottles, are deposited on food, bread, etc.

The result is that, however important contact may be in the transmission of the bacillus discharged by germ carriers, the conditions which give rise to direct contagion are not very frequent.

Consequently, transmission by indirect contagion is much more important.

From the foregoing remarks it emerges that the rôle of carriers in the transmission of typhoid fever cannot be accurately defined, but that it is much more restricted than German hygienists maintain.

It is very difficult to get definite statistics on this subject. Some writers hold that contact with chronic carriers accounted for 30 per cent. of cases of typhoid fever; others for only 2 to 5 per cent., 6 per cent. (Park), etc.

But in all epidemics, *especially in those of prolonged duration, every cause of contagion, direct or indirect, is given full play*, and thus it is often impossible to incriminate one cause more than another in the presence of such varied etiological factors.

A second conclusion to be drawn from our discussion is that among the chronic carriers of the typhoid bacillus *the most dangerous are those who are engaged in trades connected with the preparation of food.*

On perusal of the cases of typhoid contagion due to carriers, one is struck by the high number of instances in which *male or female cooks* are concerned, as well as women in charge of the preparation of food, milking, etc. Waiters or servants in a restaurant, pastry-cooks, grocers, gardeners, and men or women employed on farms or dairies are some of the most dangerous carriers.

Women especially, as we have already said, have been found to be the most numerous among the carriers. In house epidemics, therefore, when the drinking water is wholesome, one must "look for the woman," as, owing to her occupation and domestic habits, she is accustomed to handling articles of food which are consumed raw and not heated.

Contagion of this kind requires an absolute or

relative lack of cleanliness, and the fæcal contamination of the carriers' fingers and hands.

In the army contagion from man to man by germ carriers also furnishes an explanation of certain cases of typhoid fever.

Instances have been quoted in the French army, but they are more frequent in foreign armies, especially the English army in India. Strange to say, although attention has long been directed to the possible rôle of chronic carriers, cases due to this mode of infection remain rare in barracks in peace time. For various reasons direct contagion is also uncommon. The proof of this is to be found in the numerous examples of a solitary isolated case of typhoid fever occurring in a barracks and not followed by any other cases. Besides, if carriers played a preponderant part, both in the army and the civil population, how are we to explain the seasonal course of the disease, its frequency from July to October, and its rarity or absence in the cold season? How are we to explain the fact that in the army the garrisons in the north of France are almost always free from typhoid fever, whereas those in the south, on the contrary, have numerous cases of this disease? The germ carriers, however, consisting of men who have formerly had typhoid fever and who still retain their bacilli, have been distributed indiscriminately in both these areas, and their influence should make itself felt in every season.

Consequently, in the army in peace time contagion, due to carriers, is most to be feared when some of these carriers are to be found among the cooks or cooks' assistants, or among those in charge of filters or apparatus for sterilising water, the canteen women, etc.

Apart from these special cases, it may be admitted that the shaking of hands, and use of spoons, forks or cups which have been touched by the unclean hands of carriers, may disseminate the bacillus, but such cases, on close examination, are infrequent.

On the other hand—and we cannot insist too much

on this point—contagion caused by temporary or chronic carriers finds the most propitious occasions in war time, when neither fæces nor urine are confined to latrines, or washed into the sewers, or kept in pails or water-tight pits.

In spite of severe orders and constant watching, human excrement is to be found everywhere—on the ground, in cantonments, gardens and lanes, on the edges or in the bottom of ditches and in the fields—and from these sources the bacillus finds its way to man.

Whatever its original source, whether a person in the incubation stage, a patient at the onset of the disease, or with an abortive, mild or ambulatory attack, or, lastly, a convalescent or a chronic carrier, the conveyance of the bacillus to the healthy man is brought about in such a case by very varied agencies.

It is these agencies which we shall now discuss.

CHAPTER XI

INDIRECT CONTAGION BY PATIENTS OR CARRIERS—INERT FACTORS IN THE TRANSMISSION OF THE TYPHOID BACILLUS

In the hierarchy of the factors of contagion which enter into the etiology of typhoid fever, it is not permissible to dethrone some at the expense of others. It is certainly due to an excessive abuse of the German doctrine, which in itself is exaggerated, that such important agencies as drinking-water, flies, etc., were denied their proper share in the transmission of the typhoid bacillus.

The bacillus, from whatever source it may come, is carried away with the fæces and urine, and accompanies them wherever they go. When discharged outside the body, it does not find the conditions to enable it to live and grow which existed in its human medium. The soil, the air in which it is mixed with dust, water, vegetables, animals and clothes serve to protect it. The duration of its vitality in such an environment has formed the object of numerous researches, which show little agreement with one another and are sometimes divergent.

These differences can be explained by the fact that, owing to the difficulty of isolating typhoid bacilli, many observers have worked with pure cultures in the presence of sterilised earth, water, etc., thus performing experiments which in no way correspond to natural conditions. Other writers may have confused the typhoid bacillus with some other bacteria (paracoli bacilli, or *B. fæcalis alkaligenes*), which are common in fæces, manure, dung-heaps, and putrefying organic matter.

Lastly, these investigations were made for the most part at a time when the differential characters of cultures on sugar media, neutral red agar, etc., had not yet been determined.

We can, therefore, perhaps attribute only a relative value to researches on the vitality of the typhoid bacillus outside the human body.

The average period during which the bacillus survives in fæces and water-closets is from twenty-five or thirty days to five months (Galvagno and Calderini); in the soil five months (Grancher and Deschamps); in sand, street or house dust, and dry sawdust one to two months; in buried corpses fifteen to twenty days according to some observers, ninety-three according to others, etc.

All these investigations undoubtedly require revision, because the typhoid bacillus is very fastidious in its conditions of existence, and does not live long in the presence of ordinary micro-organisms.

It has been easier to study the influence of heat, cold and light on the typhoid bacillus.

It is killed instantly by boiling. At a temperature of 57 to 60° C. it is killed in an hour, but not, as a rule, after exposure for the same time to a temperature of 53° C.

When exposed to the action of the sun on dried earth it is killed in five to eight hours; porous or sandy soil is more favourable for its destruction. On cotton or linen exposed to direct sunlight it survives for from two to twenty-six hours; on black cloth from nine to eleven hours (H. Vincent).

The natural bactericidal action of the sun on the typhoid bacillus is, therefore, well established.

When deposited on linen, clothes, etc., the typhoid bacillus survives for a comparatively short time, but sufficiently long, however, to produce contagion.

Clothes, such as sheets, drawers or bedclothes, which have been soiled by a typhoid patient or germ carrier can infect persons who have to handle them, such as servants, and especially laundrywomen. Cases

of typhoid fever were formerly common among hospital laundrywomen.

Cases are on record of contagion taking place from the wearing of infected clothing. Mortchrowski has related the case of a reservist who contracted typhoid fever from wearing the shirt of another soldier who was suffering from this disease.

Thus clothes and boots and shoes worn by a typhoid patient or a carrier and contaminated by fæcal matter can infect a healthy subject. The typhoid bacillus persists from ten days to four months in books, but is killed in twelve to twenty-four hours if exposed to the light of the sun (Laubach of Baltimore). This mode of contagion by books is probably very rare.

Contagion of the soil by specific excreta is very common, especially in the country, where the general rules of hygiene are so often neglected.

In towns removal of fæcal matter is usually carried out perfectly when a drainage system exists, but imperfectly when the fæces are collected in leaking cesspits or pails. In the last two cases they remain harmful, and the bacillus which they contain may find opportunity for passing through into the soil or reaching man by the agency of flies.

Removal of excreta into the street presents the gravest dangers. This method is practised in some badly supervised towns, in the suburbs of some large towns, and some workmen's dwellings. All who pass by get infected particles caught on their boots, take them into the house and contaminate their hands.

Children, owing to their practice of defæcating everywhere, are the chief propagators of this street pollution.

In the country the contamination of the soil by fæcal matter is continually occurring. The excreta of patients or carriers are often deposited in front of the door, in the vegetable garden, or on the dung-heap. Removal of the house refuse into the street or gutter is commonly practised. The specific contamination of the soil by the typhoid bacillus finds its way

back to man by the agents already mentioned, viz. boots, clogs, bare feet, hands, vegetables, drinking-water, etc.

In barracks we find a possibility of indirect fæcal contagion by the latrines. They are often in a dirty state, and when a man goes to relieve himself he risks contaminating his boots by the side of the latrine.

Camps and cantonments, both in war and peace, provide the same opportunities for infection. If the soldiers, as frequently happens, deposit their excrement not in the fæcal trench but near it, and in addition to this the rain soaks the soil, every visit to the fæcal trench is the occasion for a more or less dangerous "microbial foot-bath." The habit which soldiers have of cleaning their boots with pieces of wood, or even with their knife, exposes them to specific contamination of their hands, especially the parts beneath their nails and between their fingers.

In camps and cantonments human excreta are only too frequently found near tents, barracks, houses, or in gardens.

War always remains the gravest efficient cause of this soil contamination, which almost invariably finds its way back to man.

The earth returns with usury the pollution which it has received. The straw used for the beds and the blankets are also contaminated. Pollution of the soil by specific fæcal matter was incriminated by Surgeon-General Derby, in the War of Secession; the troops occupying the camps abandoned by the Confederates contracted typhoid fever. The same cause was invoked in the war in Tunis; during the Russo-Turkish War, the atmosphere was sometimes rendered intolerable by the stench of the fæcal matter accumulated in the Turkish camps. At the time of the English Expedition to Egypt, the Medical Officers also noted the incredible filth of the abandoned Turkish camps.

During the South African War the extreme frequency of typhoid fever was explained by this same injurious influence of the soil, infection being attributed to the

inhaling and swallowing of fæcal dust containing the typhoid bacillus.

A similar cause was invoked by the principal Medical Officer, Millet, during a very severe epidemic in 1895 among the 14th and 15th Regiments of Dragoons during their manœuvres near Rheims on a dried-up plain covered with manure.

It is obvious that a recently dried typhoid bacillus may give rise to such infections if it preserves its vitality.

But at the present time only a very restricted rôle is attributed to this method of contagion. Some even deny it altogether.

Much more important is infection of alimentary origin, both by solids and still more so by fluids.

Typhoid fever which is accompanied by a discharge of excreta which are sometimes very rich in bacilli, readily leads to contamination of food substances by the patient or the carrier.

We have already discussed the contamination of food by unclean hands, and the conveyance of the typhoid bacillus into the alimentary canal of the healthy subject. The gathering of vegetables eaten raw (salad, radishes), the picking of strawberries or raspberries, and of fruit generally, by similarly contaminated hands, the preparation of meals, etc., all serve as occasions for depositing the typhoid bacillus in food.

There is another mode of contagion by vegetables, which is due to their being planted in a soil which has been manured with human dung, or has been watered with a mixture of fæcal matter and urine.

This is a deplorable practice, borrowed from the Chinese, which is the cause of numerous epidemic cases. The growing of cress in water similarly contaminated also offers grave dangers. In numerous countries the surface disposal of fæcal matter is carried out in a systematic manner; and this dangerous commodity is ladled out over the vegetables and the soil.

Examples have been quoted of epidemics due to the use of vegetables thus contaminated. In 1909 several cases of typhoid fever due to the consumption of raw vegetables were seen in the garrison at Vannes. The farmer who provided the vegetables was in the habit of watering them with the fæcal matter of his daughter, who was suffering from typhoid fever!

Unlike paratyphoid, which may affect animals, typhoid fever, being a disease confined to the human race, cannot be transmitted by meat, or only indirectly, *i. e.* if the meat after it has been cooked has been contaminated by the cook's hands or by flies.

On the other hand, *oysters* have been blamed, not without reason, for spreading typhoid fever. When they have been collected in the open sea, oysters are perfectly wholesome. It is by no means the same when their park is close to a harbour, and especially when they are laid close to sewer mouths and salt-marshes into which drain the residuary water of towns and villages, and with it the fæcal matter of typhoid patients and carriers. Johnston-Lavis, Netter, Chantemesse, Mosny, Remlinger, etc., have insisted upon this important cause of typhoid or paratyphoid fevers.

Netter has published striking examples of cases of typhoid fever in families or towns in which Cette oysters had been eaten. Similar cases have become so numerous that there is no need to mention them.

The increasing number of epidemics due to oysters is a striking occurrence.

In 1907 numerous cases due to the consumption of Cancale oysters were reported at Arras. Infection due to oysters also occurred at Abbeville, Mers, Treport, Eu, Sables-Olonne, etc. Several cases at Orthez, Oloron and Creusot were attributed to Cette oysters, and at Toulouse to Arcachon oysters. At Autun, which is a very healthy town, forty cases and one death were reported in October and November 1906; they were caused by the consumption of barrels of oysters which had been sent from Cette or the pond at Thaon.

The ingestion of raw shellfish, such as mussels, periwinkles or cockles, which have been kept in or collected from polluted water in the neighbourhood of sewers or in harbours, may also give rise to typhoid fever.

The special danger of oysters is to be explained by their mode of feeding. They feed on animalcules, living or dead organic particles, such as diatomaceæ, bacteria, etc., which are held in suspension in sea water. For this purpose their buccal apparatus is surrounded by four labial palps provided with vibratory cilia which draw into the stomach the food from the water. To obtain its food the oyster makes a prolonged aspiration, which enables it to pass through its digestive tube a very large quantity of water, from which it removes the principles in suspension.

If some living oysters are put in an aquarium filled with three to six cubic feet of turbid water, in a few days the water will become clear. The oyster, therefore, resembles an active filter which retains and concentrates the impurities. It is easy to understand how the oyster becomes loaded with numerous harmful bacteria, which it passes on to man when it has fed on highly contaminated water, such as that found in sewers or harbours into which fæcal matter is discharged.

Rôle of Drinking-water and other Liquid Foods.— Liquid foods, and especially *water*, play a very important part in the propagation of typhoid fever. Of all ingesta, drinking-water is the most responsible for epidemics. Ever since Brouardel's warning in 1877, countless facts have testified to the typhogenic rôle of this factor. "Drinking-water," said Guéneau de Mussy, "is an important, I might say the most important vehicle of the typhoid germ." In towns, large communities, and the army in peace time, drinking-water undoubtedly claims the first rank as the determining cause of epidemics of typhoid fever.

Like man himself, drinking-waters have their own microbial diseases, which are often due to a continuous

invasion of the micro-organism in question, while in other cases they are only temporarily contaminated by the dangerous products which they pass on to man. There are thus numerous occasions on which he may be infected, such as the swallowing of water, the consumption of raw vegetables on which specifically contaminated water has been poured, and various beverages, such as milk, cider or beer, diluted with impure water; and lastly, though very rarely, by bathing in contaminated water, of which he may absorb a certain amount.

In this respect it is obvious that water merely transmits the contamination which it has received. The causes for its pollution are very numerous, such as human excreta coming from patients or carriers, urine, laundry, sewers, etc. Surface water, whether running or stagnant, is most exposed to contamination of this kind. Deep waters, such as springs or water from the aquiferous stratum, may get pathogenic micro-organisms from the soil or latrines in their passage beneath the ground; artesian wells, on the contrary, are well protected, owing to their great depth.

Water intended for drinking does not, therefore, possess any special bacterial properties. Its purity depends partly on the geological strata through which it passes and the receptacles in which it is collected. In inhabited countries, where the pollution of the soil by micro-organisms extends to the water, the amount of germs in the water increases.

Bacteriological analysis of the camp subsoil water was made in 1892, in the camp of Hussein Dey, in which epidemics of typhoid fever were constantly occurring. Before the arrival of the troops the water was very pure, and contained only 200 ordinary bacteria per c.c. Six days later the analysis showed 770, thirteen days later 420, forty days afterwards 6960, sixty days afterwards 14,900, and three months afterwards 38,000 (H. Vincent). This is an illustration of the progressive infection of well water (phreatic

water), which is due to the presence of men on the surface of the soil, the duration of their stay, and the fæcal contamination which results therefrom.

The nature of the soil, whether calcareous, calcareous and fissured, or chalky, obviously influences its degree of permeability to the germs deposited on its surface and washed down by the rain. The soil, even at a depth of fifty metres, often effects but an incomplete purification of this water. From this point of view sandy soil is the best. But calcareous soil with large joints is permeable to the typhoid bacillus, even at a great depth.

A fissured soil which shows holes, cracks and crevices is dangerous in this respect, for it gives passage to unwholesome water and excrement diluted by the rain and deposited on the surface.

The holes of absorption into which a stick can be thrust with difficulty serve as passages for the surface waters (Martel), and so permit of the contamination of the subsoil water.

It is a well-established fact at the present time that, thanks to the permeability of the soil and the existence of holes for absorption, fissures and crevices, as well as subterranean currents, typhoid fæces may be very contagious, in spite of their being deposited at a great distance from the point of emergence of a spring. All the springs which supply Paris with drinking-water are exposed to this cause of infection. Fæcal pollution of one of the reservoirs, eight to ten kilometres from the spring, may contaminate it, especially after heavy rain. Rigorous and efficient protective measures have, therefore, been taken.

Waters of the Vauclusian type, *i. e.* those which, after running open to the air and so exposed to every possible cause of pollution, disappear into the soil and sometimes emerge again in a remote district, are especially dangerous (Martel).

The inhabitants of Sauve, in the department of Gard, thought they had discovered a spring when they were really drinking the water of their own sewer.

In the Jura Department, says Martel, all the springs are polluted by manure, night-soil, and the carcases of animals. A well-known example of a dangerous outlet is that of the Loue spring, which is merely the water of the Doubs, which disappears at Arcon. In 1901, when a fire destroyed an absinthe factory at Pontarlier, the spirit flowed into the Doubs, with the result that the Loue spring acquired a taste of absinthe.

Very numerous examples of springs with a reputation for purity (Avre, Vanne, etc.) have been shown to communicate with streams which flow sometimes on the surface of the soil and sometimes below. Thus the Lunain disappears after a course of ten to fifteen kilometres.

The typhoid infection of surface and underground waters is brought about by human fæces and urine deposited on the surface of the ground in pits near wells; it is also caused by cultivation of the soil and the dangerous practice of manuring it with dried human dung. The rain sweeps the ground, follows its declivities or infiltrates the soil, carrying pathogenic germs with it into the subsoil water.

Sometimes the well is in the immediate neighbourhood of a privy (P. Brouardel); certain towns, like Cherbourg, still show examples of the kind. Sometimes the laundry in which the linen of typhoid patients is washed is close to the spring from which the inhabitants get their water, when there is really a subterranean communication between the spring and the laundry. Water in ditches situated some hundred metres away from a spring may be seen to present oscillations of the same level, showing that both are connected with one another. Human residues and excreta percolate from one to the other.

We have given only a brief sketch of the commonest modes of adulteration of drinking-water. They easily explain the conveyance of the typhoid bacillus, its absorption sometimes in large quantities by the inhabitants of a town, village, barracks or school, and

the occasionally formidable outbreaks which result therefrom.

What becomes of the typhoid bacillus when it is discharged into water? Does it multiply, or retain its vitality?

All bacteriological investigations have shown that the typhoid bacillus hardly ever lives more than four or five days; sometimes it is impossible to find it after the third day.

The typhoid bacillus, therefore, does not long survive in drinking-water.

Moreover, the influence of diffuse light, and especially of the direct light of the sun (on rivers, ponds and lakes), has an energetic sterilising action. In clear water the bacillus is killed in four to six hours by the solar rays, and in eight to nine hours in turbid water. The actinic rays possess the most active power (death in two and a half to three hours), while the heat rays have a much weaker effect (more than fourteen hours) (H. Vincent).

But so long as it persists in the water the typhoid bacillus retains its pathological activity. Besides, it may be continuously poured into drinking-water by excreta, urine, laundry, etc., and so keep up the dangerous pollution of the water.

Numerous epidemics which have occurred in large towns, villages, barracks and cantonments can thus be explained by the consumption of polluted water.

The idea, therefore, of the pathogenic rôle of drinking-water still maintains its value in etiology.

The theory of germ carriers simply completes it, inasmuch as the pollution of water may be due not only to the excreta and urine of patients suffering from typhoid fever, but also to carriers as well.

In war-time contamination of drinking-water depends upon that of the soil.

In his hurry to relieve himself the soldier deposits his excrement without any precautions in ditches, on the side of the road, near wells, springs or water-courses, etc., and washes his clothes in the gutter.

Fæcal matter accumulates on the ground in enormous quantities, especially in stationary warfare, like the great war at the present day.

The result is that bacteriological examination rarely shows a water of wholesome quality. Most waters are intensely infected by B. coli and putrefactive microbes, which are constant associates of the typhoid bacillus.

Consequently, in war time one should *a priori* regard all drinking-waters with suspicion if they have not been thoroughly sterilised.

Paris has several times given a proof of the very important rôle of drinking-water in the epidemiology of typhoid fever. Brouardel, Thoinot, Chantemesse and Widal, Lancereaux and Mosny, demonstrated long ago that the distribution of Seine water was followed by twice to six times as many cases of typhoid fever in the hospitals. In 1894 and in 1900 the Vanne water, which was polluted at its source, was the starting-point of serious epidemics.

Dr. Hoel, Director of the Bureau of Hygiene at Rheims, has drawn attention to the epidemic of 1885, with 1500 cases and 142 deaths, which occurred for the most part in the Cérès quarter, inhabited by the working population, which drank almost exclusively well water into which cesspools soaked.

One of the most conclusive examples of the influence of water and its persistent action is given almost every year by Marseilles.

In 1907 this town had more than 3000 cases of typhoid fever with 423 deaths. In 1913 an equally severe epidemic occurred. Marseilles receives its water supply from the Durance, whose stream is exposed to the air and collects on its course human excreta, laundry water, etc. It is also supplied by the Rose and Huveaume water, the quality of which is equally doubtful.

Cherbourg, whose civil population and military and naval forces have frequently suffered from typhoid fever, owes its defective sanitary condition to the use

of the Divette water. From 1878 to 1887 its naval and military forces had 4162 cases, with 400 deaths! In February, 1909, a new epidemic occurred, with 300 cases and 60 deaths, among the soldiers and sailors. The river Divette, which is nothing better than a sewer, had been polluted on January 6 by the excreta of a woman suffering from typhoid fever, and continued to be contaminated throughout her illness. The first cases of typhoid fever occurred on January 25.

The epidemic of Saint-Brieuc (June 1909), in which about 900 civilians and 160 soldiers were attacked, was due to the washing of a typhoid patient's clothes in a laundry, the water of which ran into a stream which supplied the town.

The terrible epidemic of Avignon in 1911, and those of Marseilles in 1913, and of Montauban in the same year, were caused by the impurity of the drinking-water.

In the garrisons in Algeria, Tunis and Morocco, where prior to specific vaccination typhoid fever used to rage with an appalling violence, bacteriological examinations carried out in the laboratories regularly showed a considerable pollution of the drinking-water. In certain towns, indeed, systematic water analysis, by revealing an unusual pollution, enabled one to foretell epidemics which actually occurred a fortnight later. At Blida in 1893 a soldier, who wished to be sent to a convalescent hospital, intentionally swallowed a large quantity of condemned water (Oued el Kebir). He contracted typhoid fever from which he died.

The study of the epidemiological facts observed in every country, including England, the United States, Italy, etc., as well as in France, has fully confirmed the extreme importance of the bad quality of drinking-water in the etiology of typhoid fever, the immunity which those enjoyed who did not drink the unwholesome water, and the occasionally enormous incidence of the disease among those who did.

Beverages derived from water or containing water, such as ice, Seltzer water, lemonade, cider and milk,

may give rise to contagion. Epidemic cases due to the consumption of impure ice were reported at Vannes; eight officers who attended a banquet in which they partook of ice which came from a part of a river where several sewers opened, contracted typhoid fever. Two succumbed. Two, who had drunk beer, escaped (Major Dorange, 1898).

Milk is an equally dangerous element of contagion when it is drunk unboiled. Its contamination is due to its having been taken from the cow, or poured into a vessel by carriers with unclean hands, or to its having been collected in receptacles washed with dirty water, or diluted with water of this kind which contains the typhoid bacillus. In England Duncan recorded in 1873 the severe epidemic at Crosshall, which occurred among 500 families who had consumed milk infected by impure water taken from a stream into which excreta were discharged. The families who had drunk milk from another source escaped.

Guéneau de Mussy related in 1881 the history of the epidemic in Marylebone, which claimed 300 victims in a healthy quarter of London. The milk came from a farm in which there had been a case of typhoid fever. The farm well received the leakings of a cesspool. A sanitary inspector, who doubted that this was the cause of the contagion, drank the suspected water and contracted typhoid fever.

A very severe epidemic due to contaminated milk was observed in 1913 at Jargeau (Loiret). It gave rise to a high incidence of cases in certain families (Grancher).

Rôle of Flies.—The part played by flies in the propagation of certain infectious diseases has been proved for a long time. Attracted by the typhoid patients' excreta, vomit, urine, blood and pus, or by latrines and dung-heaps, *flies* carry off the typhoid bacillus on their legs and proboscis and convey it elsewhere. The typhoid bacillus lives in the intestines of flies (Celli, Odlum), which are therefore true bacillus carriers. They become filled with infectious microbes,

either some distance away or in neighbouring houses, and thus, laden with elements of contagion, they carry them into kitchens or canteens and deposit them on the food, fruit, pastry, milk, and the hands and face. They are contagious, not only by their legs and proboscis, but also, and perhaps most of all, by their excreta, for they defæcate very frequently.

Their danger is also due to their number, which may be extraordinary, especially in hot seasons or climates. *We have thus undoubtedly an explanation, in part at least, of the predominance of typhoid fever during the summer and autumn,* which are favourable seasons for the multiplication of flies, as well as in the towns or garrisons in the south of France, in Algiers and Tunis, Morocco and all the countries along the shores of the Mediterranean, where flies swarm in such abundance. This also explains why the houses of the poor, in which attention to cleanliness and hygiene is too often neglected, and which serve as a home for myriads of flies during the summer, are frequent foci of typhoid fever.

Attention has been called to contagion by flies, to their excessive frequency and their dangers in camps, especially in war-time, by army medical officers, during the expedition to Tunis, the Turco-Russian War (Dobroslavine), the war with Cuba, the Transvaal War, the Russo-Japanese War, and the war of the Allies with the Central Empires.

The "plague of flies," as an American doctor, Sternberg, called it, was the cause of the great frequency of the cases of typhoid fever seen in the Spanish-American War. Being inseparable companions of men and animals, *flies act as a powerful and formidable intermediary, and as a factor of contagion of the first rank.*

The English army doctor, Odlum, published in 1908 the account of a very severe epidemic which occurred in a regiment of Highlanders at Nasirabad.

The usual methods having failed, a systematic destruction of flies was carried out. The epidemic

which had ceased in July and August, returned when the flies reappeared. A search was then made for the breeding places of the flies, especially in the fæcal trenches, which were disinfected, and "not a single case more of typhoid fever was observed."

We need only mention, in passing, the rôle of fleas and lice, which has sometimes been invoked, but never actually proved. The relative rarity of the bacillus in the blood of the typhoid patient prevents us from supposing that this mode of active infection is frequent or even possible.

CHAPTER XII

CHARACTERS AND EVOLUTION OF EPIDEMICS ACCORDING TO THEIR CAUSES

In the previous chapters we have discussed the respective influence of the various factors in the etiology of typhoid fever. It would not be accurate to attribute an equal importance to each of these modes of contagion. Some there are, such as contagion by unboiled milk, oysters, shellfish, clothes, and raw vegetables, which, though fairly often observed, have not, however, the same frequency as others, such as the influence of adulterated drinking-water, contagion due to flies, direct contagion from man to man by patients or carriers, etc.

Though its importance has been discredited by some hygienists, the rôle of drinking-water, especially in big epidemics, undoubtedly still claims the first place. The substitution of a naturally or artificially pure water for one that is contaminated has been followed by an unprecedented reduction, or even by the almost complete disappearance of typhoid fever in a large number of towns. It is especially in the soldier, who reflects so faithfully the sanitary state of a town, that, thanks to the active and persevering measures demanded and obtained by army medical officers, a considerable improvement in sanitation has been obtained.

Brussels, London, etc., like Paris, have shown a very pronounced drop in their typhoid incidence and mortality, following the installation of large and expensive works for supplying pure water.

But drinking-water is obviously not the sole factor.

It would be imprudent to suppose that a pure water supply would rid the civil population and army for ever of typhoid fever.

In a number of cases bacteriological and chemical analysis of the water proves its good quality, whether it is that the cause of its infection is transient or the culture has been taken too late, or that the water really is pure.

If water can be excluded, in the presence of a diffuse epidemic without any appreciable co-ordination between the cases in time or space, one should think of one of the other causes which we have studied.

During the hot season, and especially in poor families, flies play an important part.

Investigation should be made as to contagion by one or more carriers employed in an occupation connected with the preparation of food.

In such cases the essential element of the contagion can be detected by the inquiry made and the bacteriological examination.

In the presence of an epidemic and with the object of cutting it short as quickly as possible, it is necessary to weigh the facts impartially, to construct a map and a table house by house of the cases observed, of their distribution, succession and successive onset. This simple analysis by means of the map may furnish very interesting information. Sterile or ill-founded hypotheses should be avoided, and laboratory help should be enlisted to detect the true factors.

It is important to know that when an epidemic has taken on a prolonged course, it is impossible to attribute it to a single factor of contagion. All causes and methods of transmission may be associated, such as direct contact with the patient, consumption of food which has been prepared by a servant who has neglected to wash his hands after attending a typhoid patient, contagion by a carrier who has also unclean hands, conveyance of the germ by that dangerous carrier the fly, by non-sterilised linen, a rectal thermometer or bedpan which has been con-

taminated by the stools or urine of a patient and not disinfected. These conditions combine with one another and become associated with the initial or fundamental cause to keep up the supply of epidemic cases and prolong their effects.

The *course* and *evolution* of the epidemics themselves owe their special character to the cause which provoked them. It has been well proved that epidemics due to water are widespread. They chiefly affect persons who have had no previous attack which could have immunised them. In towns, new arrivals, including soldiers, travellers and servants, are specially affected.

Furthermore, epidemics of this kind due to drinking-water have almost always a sudden and explosive onset, affecting a large number of individuals all at once, and in a short space of time, often within two or three weeks.

Such was the case in the epidemic of Auxerre (1884), so well studied by Dionis, which gave rise to 800 cases; in the Caterham epidemic (in the county of Surrey) in 1879, which affected 352 persons simultaneously; in the epidemic of Chatillon-sur-Seine (December 1883) described by Bourée; in the epidemics of Cherbourg and Saint-Brieuc in 1909; in the celebrated epidemic of Avignon in 1911, which gave rise to more than 1000 cases of typhoid fever, etc. These epidemics may last several months.

It is also observed that the first cases begin about fourteen to fifteen days after the use of impure water, a time which corresponds to the minimum duration of the incubation of typhoid fever. It is exactly the same in the cases of accidental absorption of the typhoid bacillus in laboratories. But, as the incubation period is not the same for all, a series of later cases may occur, twenty, thirty and even forty days, even after laboratory contagion.

Epidemics due to the use of unboiled milk contaminated by water, carriers, or flies show a similarly sudden and simultaneous character. The epidemic

is at first limited to single individuals, to the customers of the infected dairy, or to families which make use of the milk, and it affects those exclusively who have drunk it unboiled.

In like manner the consumption of oysters or shellfish by a number of persons may have a similar result.

It has often been noticed, and Netter has quoted some conclusive proofs, that ingestion of water or food contaminated by the typhoid bacillus causes on the same or following day an attack of indigestion accompanied by fever and diarrhœa.

Typhoid fever appears later at its ordinary date. It seems that this initial diarrhœa, which might indicate invasion of the organism by the typhoid bacillus, is more probably due to the absorption of other bacteria associated with the specific bacillus, such as proteus, the enterococcus of Thiercelin, bacteria of putrefaction, etc.

Epidemics due to contagion by flies show a sporadic character, without any apparent connection between the cases, and the history, as well as the search for carriers and water analysis, are unable to explain them.

Cases of typhoid fever due to contagion by carriers sometimes appear in an epidemic form, usually of limited extent, but more frequently in a sporadic (or epidemic) form. These cases are grouped in the same house, the same family and the same community. Their onset is less sudden than that of epidemics due to water, and their extent is less considerable.

They succeed each other irregularly and are abnormally prolonged, in every season, both winter and summer, with sometimes a long interval between each and without any obvious connection.

Their frequency depends, indeed, on the frequently intermittent discharge of bacilli in the excreta and urine, on their amount which is always less than in the actual course of typhoid fever, on the existence of attacks of diarrhœa, on the varying degree of cleanliness of the germ carrier, on his occupation, and the association of special circumstances which are very fortunately

not always combined, so that the chances of contamination are restricted.

It is needless to state that flies, those formidable agents for the transmission of pathogenic microorganisms, and especially the typhoid bacillus, make their influence felt in summer and autumn. The accumulation of excreta and only a slight fall in the temperature may prolong their existence, not only in hot countries, but also in temperate climates.

During the war of 1914–1916, flies were sometimes found in the trenches and cantonments during part of November.

CHAPTER XIII

PROPHYLAXIS OF TYPHOID FEVER

Prophylaxis of Favouring Causes

THE description of the ordinary modes of contagion in typhoid fever will better enable us to deal with the various prophylactic measures against this infectious disease.

Considerable importance was formerly attached to the favouring causes of this disease. Although the bacillus remains the only responsible agent for this process, it will be well to consider these secondary factors and to endeavour in practice to restrict their action as far as possible.

We will therefore study the prophylaxis of the accessory causes which favour the outbreak of typhoid fever. *Specific or microbial* prophylaxis will then be discussed.

Among the conditions which most predispose to an attack of typhoid fever, age, fatigue or overwork and the influence of heat are among the most important.

Age, especially adolescence and the age between eighteen and twenty-five are predisposing factors which we cannot guard against. Nevertheless, they stimulate us to multiply during this period all the measures for removing or destroying the typhoid bacillus (the seed) or of immunising the susceptible subject (the soil). The same advice is applicable to young persons of both sexes who are devoted to sport and indulge in it to excess, which frequently leads to loss of flesh and cardiac or renal complications, and to those who are preparing for examinations and

competitions without sufficient hygienic precautions or the necessary relaxation.

In the army, experience has shown, contrary to certain apprehensions, that the soldier may be incorporated at the age of eighteen to twenty on the condition that he undergoes a progressive training. It is therefore necessary to confide experienced medical men with the hygienic supervision of young persons of both sexes who are devoted to sport, as well as of soldiers who have recently joined the army. Their physical education should be conducted with prudence, otherwise they will be more liable to infectious diseases in a severe form. A methodical and progressive training should be insisted upon.

For this reason the societies for physical education, military education and gymnastics should be warmly encouraged, for they help to form an energetic and supple race, which is better able to resist not only fatigue, but also the morbid conditions which are so liable to attack young persons.

Owing to the influence of the seasons on the appearance of certain epidemic diseases, the spring may be regarded as the most favourable date for the enrolment of young soldiers in peace time. In the Colonies it is best to mobilise soldiers in the winter.

Expeditions which begin during the hot season, or even at its commencement, have been paid for at the price of violent epidemics of typhoid fever.

It should be added that the prevention of the disease by anti-typhoid vaccination diminishes in the highest degree the influence of the favouring and determining factors which we have studied, just as the preventive and curative use of quinine, by creating a sort of medicinal immunity, has considerably reduced attacks of malaria and diminished the importance of its occasional or determining factors.

Side by side with physical overwork, demoralising causes and depressing emotions concur in predisposing to typhoid fever, and especially to grave attacks. Every practitioner should be familiar with these causes.

The general hygiene of the dwelling, its ventilation, the exposal of the rooms to the light, especially of the bedrooms in which man passes at least a third of his existence, the general cleanliness of houses, schools, factories, etc., and especially that of kitchens, dining-rooms, latrines and court-yards, and their proper ventilation, all constitute a collection of hygienic rules which are applicable not only to the prophylaxis of typhoid fever, but also to that of tuberculosis.

The same remark applies to barracks. For this reason it may be laid down as a principle that *the best position for barracks is in the heart of the country.*

Life in *camp* is in every respect more wholesome than in towns in which infections of every kind are often accumulated. The mess-rooms, latrines, urinals and punishment cells should receive special attention from the regimental medical officers.

The child should be instructed in individual cleanliness, including that of the face, mouth and hands. Regular washing of the hands, especially before meals, should be a constant habit and a sort of reflex for every one.

This early education, in spite of its importance, is too often neglected, especially in the country. It should form the subject of a few lessons in elementary hygiene by the school teacher. It should be taught early in life, so that it should not be forgotten that cleanliness is one of the manifestations of self-respect.

In this exposition of the prophylactic measures applicable against accessory or favouring causes we can obviously give only general indications. A detailed description is included in the rules relating to microbial prophylaxis, properly so-called. For this reason it will be sufficient to mention the favourable effects of a careful alimentary hygiene, and to recommend the use of pure water and wholesome food protected from dust and contamination of every kind.

In camps and cantonments, in peace time, and in the trenches, huts, and temporary or permanent encampments during war, one must combat the

formidable danger resulting from the infection of the soil by human or animal excreta, urine, kitchen refuse, residues of all kinds, as well as by dung heaps and putrefying matter which may harbour flies and their eggs. Such measures constitute indirect prophylaxis of the utmost importance.

Therefore, before occupying a village or a cantonment a careful inspection should be made, house by house, when possible—which the conditions of a war of movement do not always readily allow—a note should be made of unwholesome and badly ventilated houses, with their accumulations of manure which serve as huge breeding-places for flies. They should be cleaned, disinfected, washed and all the filth cleared out. The best means of profitably disposing of dung-heaps is to scatter them as soon as possible over the fields or the soil that is going to be sown, at a sufficient distance from inhabited dwellings.

If this measure cannot be carried out, they should be disinfected or even burnt. The health of the troops is the first consideration. The manure-pit and pond into which the rainwater and liquid manure drain must be filled up and the ground disinfected.

In permanent camps the ground should be hardened, and if possible paved, wherever the soldier is living and moving about, viz. the huts and tents, and at all events the sides of the road.

All depositing of manure should be forbidden. Incinerators should be built for destroying kitchen refuse, rubbish and filth, which may putrefy and attract flies.

Whenever the conditions of the site permit, latrines with drains and a water flush should be installed.

The hygienic arrangements of a camp should as far as possible resemble those of a town.

In the absence of a drainage system orders should be given to erect latrines with pails under strict supervision, or deep trenches which must be carefully disinfected twice a day in summer and once daily in winter.

The huts and tents should be ventilated during the day. The approaches to them must be strictly clean. Night latrines render real service not only in barracks, but also in cantonments and camps.

Should knowledge of the ordinary modes of propagation of typhoid fever be the exclusive possession of the doctor and hygienist? There is no doubt that if spread among the public in a suitable way it would have a good effect on the diminution of typhoid fever.

Education of the population in hygiene can only be carried out with the active assistance of public authorities and the participation of the medical profession. It should form an integral part of the instruction given to children (H. Vincent), and should be repeated in the case of the adult. In this way every one will be properly schooled in the principles of hygiene and become the conscious collaborator of the medical man.

One of the most important causes of the spread of epidemics of typhoid fever is to be found in the ignorance or indifference of the public. For this reason summary instruction, imparted in informal addresses given by a medical member of the Municipal Board of Health, the District Commission or the Council of the Department would serve to popularise the succinct principles which every one should know, relating to the parasitic nature of contagious diseases and their modes of propagation.

Popular instruction imparted at school, at the town hall, in the workshop or at home, will have far-reaching effects and be a valuable help to the laws and regulations on the prophylaxis of infectious diseases.

An immediate inquiry into the causes which started an epidemic, bacteriological study of the stools, examination of the blood by culture, or, failing that, by the serum test, will be of considerable help in the struggle against typhoid fever.

Bacteriological study alone can indicate the cause of the disease and thereby enable immediate measures

to be taken for the isolation of the patient, disinfection of the stools, linen, latrines, etc.

It will become possible by means of sanitary stations and laboratories of this kind to restrict the frequent cases of contagion from man to man, to exercise supervision over drinking-water, and to control its bacteriological quality.

Except in the army, in peace as well as in war time, in which all beverages are analysed and forbidden as soon as they are found to be unwholesome, bacteriological examination of water is practised in only a few towns.

There is another institution which is absolutely necessary, viz. a sanitary register of parishes and houses, with a record of all the cases of infectious diseases, and especially of typhoid fever. The cases of illness would thus draw the attention of the Boards of Health and facilitate the determination of the cause of epidemics.

CHAPTER XIV

SPECIFIC PROPHYLAXIS OF TYPHOID FEVER

The progress of epidemiology has taught us the various stages through which the bacillus passes to reach man, as well as the direct causes and indirect factors in its transmission.

This knowledge having been acquired, the first measure in an epidemic consists in an exact bacteriological diagnosis (typhoid fever or paratyphoid), and a minute and as complete an inquiry as possible as to the first case and those which followed it, both at once and at a later date; in a word, as to the collection of conditions which may foster an epidemic or endemic state.

In dealing with an epidemic, which, after all, is only a collective disease, the epidemiologist should behave like a doctor with his patient. He should discover as soon as possible the exact nature of the affection, by having a culture taken early from the blood, both of patients and suspected cases,[1] and should then endeavour to discover the one or more causes of the disease and employ the appropriate remedies.

The prophylaxis of typhoid fever should have in view: (1) The patient. (2) The persons about him. (3) Carriers. (4) All inert and inanimate agencies which are capable of carrying the typhoid bacillus and passing it on to man.

Let us now discuss these various elements of contagion.

[1] It appears advisable to remind the reader that the earlier the blood-culture is taken the more likely it is to be positive. The culture should be taken again, and a larger quantity of blood should be used when the first culture is negative.

Every typhoid patient, including suspected cases, should be isolated as early and completely as possible. This isolation should precede notification, which is compulsory. It is unwise to await the confirmation of the diagnosis by the clinical symptoms and bacteriological examination before isolating the patient. In the case where isolation has not proved necessary, no harm results, but in the event of a positive diagnosis it must be remembered that the typhoid bacillus is present in large numbers in the stools, not only at the onset of typhoid fever, but even before the appearance of the first symptoms.

It will be necessary, therefore, to exercise supervision over the patient's household who may already have been contaminated.

All delay in the isolation of patients and suspected cases may expose a large number of persons to contagion, especially those in the immediate neighbourhood of the patient. Isolation should be completely carried out in the army, especially in war time. The patient should be placed under observation and removed without delay with a provisional diagnosis, if the febrile symptoms and digestive disturbances persist or get worse. It is right, however, to mention that in war time it is very common to observe transient infections which clear up in a few days as the result of rest, purgatives and restricted diet, and have no relation with typhoid or paratyphoid fevers. It is a peculiar fact which is worth noting, that during war time infections of all kinds which are in no way related to one another are apt to be accompanied by gastro-intestinal disturbance.

Blood-culture and, if necessary, cultures of the excreta and vomit, will help in the diagnosis.

In hot climates and in the East, and all the countries along the shores of the Mediterranean where malaria, papatacci fever (three-day fever), recurrent fever and Malta fever are prevalent, these diseases very often assume a typhoid disguise which may mislead the doctor. Laboratory examination will lead to the

adoption of the prophylactic measures required by an exact diagnosis.

No rational prophylaxis, therefore, can be carried out either in the army or in the civil population without aid from the laboratory.

As soon as the diagnosis of typhoid fever is established, prophylactic measures should be rigorously employed. After *isolation* of the patient disinfection should be carried out.

This applies to everything that has been contaminated by fæcal matter, urine and expectoration of the typhoid patient, and to the dead body as well. Disinfection of the walls, the air and the room in which the patient has been under treatment is of less importance. But disinfection of the floor,[1] which is frequently contaminated by excreta, and also of the linen, spoons, glasses and bath water should never be neglected.

Disinfection should also apply to persons who are looking after the patient. The relations and nurses may transmit the bacillus to those about them by means of their hands or their clothes, especially if they are in the habit of preparing the meals. They may also themselves become the first victims of their negligence or forgetfulness, if they are not vaccinated. Hands and clothes should, therefore, be washed or disinfected as often as is necessary.

Neglect of the *compulsory notification* of typhoid fever ordered by the law of February 15, 1902, and the decree of February 10, 1903, has too frequently entailed an extension of the disease and the omission of local measures of disinfection.

It appears certain that cases are not notified as often as they should be. Medical men have put forward the uselessness of this notification, because it is not always followed, especially in the country, by disinfection. But disinfection does not constitute the entire prophylaxis of typhoid fever, and it is for the practitioner to have the measures which we have

[1] *Eau de Javelle*, a hot solution of caustic soda and 5 per cent. solution of carbonate of soda form excellent disinfectants for floors.

already described carried out without it being necessary to have recourse to official intervention.

The rarity of notifications has also been attributed to the fear of hurting local trade by placing a ban on a business house, or to the infected districts being put out of bounds for men on leave by the military authority. Soldiers too frequently bring back to barracks the infectious diseases which they have contracted during the stay in their village. Such serious consequences demonstrate the absolute necessity for notification of typhoid fever and other contagious diseases.

If it were made after the doctor had formally expressed his opinion on the case, by the head of the family, or in his default by the lodger, as is the rule on the declaration of births, the notification would give rise to fewer objections.

As regards the persons who are looking after the patient or are in his immediate vicinity, arrangements should be made to vaccinate them; they should be impressed with the necessity of washing their hands carefully, wearing rubber gloves, changing their overalls or smocks when they are contaminated; and of never eating or putting their hands in their mouth in the patient's room.

Prophylaxis with regard to carriers.—No regulations or laws have been laid down in France with regard to carriers. The Academy of Medicine, nevertheless, in 1909 and 1910, expressed its authoritative opinion on this delicate question.

The existence of carriers undoubtedly complicates the prophylaxis of this infectious disease. The difficulty arises from the fact that these latent carriers, who are moving from place to place and so disseminating unconsciously the typhoid bacillus, are not as a rule revealed by objectively appreciable signs. It is only by the cultivation of their excreta that the pathogenic micro-organism can be discovered, and even then it is very difficult to isolate.

What measures should be adopted against this

source of contagion? Carriers obviously cannot be compelled to submit to compulsory isolation, or even to legal regulations obliging them to take minute precautions with regard to their excreta and urine. At least, nothing has been done hitherto in this direction. The gravity of the problem cannot be hidden. It is complicated by the fact that certain carriers remain so all their lives.

There are, indeed, no legal remedies for carriers. It is only in cases in which it is proved that they had a culpable intention of doing harm that the law could be applied to them.

Prophylaxis consisting entirely in investigating carriers and disinfecting their excreta could not cut short an epidemic. When undertaken locally in Germany in 1904, with an abundance of precautions and laboratory examinations which would render it inapplicable in an extensive area, this method seemed to diminish the frequency of typhoid fever in the region under supervision, but not in proportion to the effort expended.

All that it appears possible and useful to do consists in informing the carriers themselves of the dangers of their fæces and urine, and of the manner in which they can make themselves inoffensive, viz. *by careful washing of their hands after defæcation and micturition*, with prohibition to deposit their excreta near wells, springs, or in gardens, etc., sterilisation of body linen by boiling water, and giving up every occupation connected with the preparation of food. Carriers should be induced to take these precautions in their own interest.

Have there not been instances of cooks who were found to be disseminating typhoid fever, and were consequently turned out of all their situations? Some of them, however, to obtain a home had the excreta of a healthy person analysed in place of their own!

With convalescents from typhoid fever we are better able to cope. The recent recollection of the danger they have run, and the advice or apprehensions

of their friends, who have been enlightened by the doctor as to the contagious character of germ carriers, ensure precautions being taken for the time being. The difficulty is to enforce their observance for a sufficiently long period.

Persons suffering from biliary lithiasis, chronic jaundice, etc., should be told that they are, or may be, typhoid or paratyphoid bacillus carriers, and that the most serious results may occur if they follow an employment connected with the preparation of food or cooking.

But in actual practice the principle of individual liberty will doubtless long be a stumbling-block to the valuable measures which society claims against carriers.

We must, therefore, try to find a method by which the bacillus carrier can be effectually freed of the bacilli lodged in his gall-bladder, renal pelvis and bladder. There need be no question of cholecystectomy, which has been performed without causing the bacillus to disappear.

Specific vaccination of the carrier, even with the bacillus isolated from his stools, has not given a definite result. It is the same with the use of lactic ferments.

One is therefore led to conclude that *the best prophylaxis for the contagion due to carriers consists in preventive vaccination of all persons living in contact with them.*

Water and other Beverages, Food, Flies, etc.

Drinking-water is of great importance in the etiology of epidemics of typhoid fever. In the rural population, or small towns, in armies on manœuvres or on active service, well-water as a rule is responsible for this method of diffusing the germ. Every well and every spring ought, therefore, to be surrounded by a zone of protection against pollution by dung-heaps, latrines, etc. But the difficulty of realising such a measure in private property is very great.

The civil authorities, however, are entitled to impose a supervision over the *parish wells*, and to demand an adequate zone of protection. They may also insist on the closing of the wells in public establishments, hotels, restaurants, inns, cafés and bars, which have been found to be contaminated on bacteriological examination.

For the same reason the military authority forbids the troops access to these establishments. But in war time, in which half-measures are insufficient, we can but approve of orders which formally condemn infected wells, springs, streams, etc., and which *command a systematic sterilisation of all the water drunk by soldiers.* Various methods described in textbooks on hygiene (*v.* G. H. Lemoine, *Hygiène Militaire.* Paris, 1911) show how this may be carried out. The simplest, most practical and most efficacious method is treatment by *Eau de Javelle.* Alkaline hypochlorites added to water so as to give off one milligramme of active chlorine per litre of water form an excellent sterlising medium. The amount of chlorine must always be first estimated by a chemist or dispenser, as its amount varies considerably according to the origin of the *Eau de Javelle.*

For this reason calcium hypochlorite tablets of varying size have been advocated for the sterilisation of the water to be purified in precise amounts of one litre, ten litres, etc. (H. Vincent and Gaillard). Water purified by hypochlorites should not have a perceptible taste, but only just an extremely faint odour. The typhoid bacillus and the paratyphoid bacilli as well are killed on the average in ten minutes' time.

Numerous towns in the United States have regularly employed this process without any ill-effects. Free chlorine does not appear to attack lead or earthenware pipes, as these are protected by the calcareous coating deposited by water. At Paris treatment by *Eau de Javelle* is employed wherever the quality of the water becomes doubtful. It is therefore a method of very great and practical importance, costing little, inoffensive, and very efficacious.

We have said that other beverages than water, e. g. *milk*, can convey the typhoid bacillus. All families should always be urged to boil their milk, the danger of tuberculous contagion being added to that of typhoid and paratyphoid contagion. By having the milk boiled this double danger is easily remedied.

Cider, *perry*, *sour wine* and *beer* may also give rise to typhoid fever if they are diluted with contaminated water, or are contained in unclean vessels which have been washed with dirty water, or, lastly, if they are handled by carriers.

During the war of 1914–16 bacteriological analysis of certain beers from the north of France, which had been drunk by our soldiers, showed a very serious bacteriological pollution and an extraordinary number of micro-organisms.

The consumption of cider and of *sweet*, non-fermented wine to which impure water has been added is also not without danger.

The only method of prophylaxis consists in the analysis of these beverages and their prohibition, with penalties in case of disobedience on the part of the dealers, whoever they may be, and whether they have received a licence or not, but especially proprietors of public-houses, cafés, inns and restaurants.

Placards and notices put up throughout the villages, cantonments, etc., should call the attention of the populace and the soldiers to the harm and dangers of beverages of this kind.

The prophylaxis of typhoid fever due to *food* contaminated by fæcal matter or urine depends upon the causes which provoke this contamination. It seems unnecessary to remind the reader of the rôle of vegetables, fruit, radishes, salad, cress, strawberries, cucumbers, tomatoes, etc., to which the bacillus may have been brought directly by surface disposal, or indirectly by manure in epidemic times, or in districts in which typhoid fever is prevalent; it should be hardly necessary to order abstention from raw

vegetables, etc., or at least to subject them to careful and prolonged washing in cold water. It should also be noted that flies may convey the germs to them later.

The important question of surface disposal of human manure—a practice employed in a large number of agricultural regions—is closely connected with infection of food, as well as of the soil in market gardens, and of drinking-water, when the ground is fissured and provided with wells or cesspools.

The Academy of Medicine energetically condemned this unwholesome and deplorable custom in 1900. The *Law of February* 15, 1902 (Art. 1), forbade the *surface disposal* of human manure within the protective area surrounding wells; Art. 28 of the same law enacted penalties against any one who let excrementitious matter be introduced into well-water. Municipal authorities are, therefore, armed against surface disposal. But this repulsive practice is profoundly anchored in country habits, and habits are often stronger than laws. In fact, no legal measure has ever been taken against the use of human fæcal matter and urine, which has been the cause of so many cases of typhoid and paratyphoid fevers and of many deaths. It is at least necessary for existing legislation to be completed, reformed and strengthened, and for surface disposal to be forbidden in market gardens in which vegetables eaten raw, as well as strawberries, are grown, and also at a distance less than a hundred metres from drinking-places, springs, wells, etc., used for drinking purposes.

Lastly, prohibition of the use of the excreta of patients in private houses or hospitals should be equally absolute.

Epidemics of typhoid fever due to oysters have formed the subject of numerous reports. The supervision and regulation of oyster parks, and the prohibition to lay them in harbours, near the shore, or sewers, or to keep them in nets plunged in these germ-saturated waters, have several times been de-

manded (Mosny), but without effect. For this reason Fabre-Domergue has suggested the placing of oysters in pure sea-water for a few days to enable them to get rid of these harmful germs. It is to be hoped that such wise and useful measures will receive the support of the sanitary authorities.

As we have said, flies form important agencies for certain germs, such as the typhoid bacillus, the paratyphoid A and B bacilli, the cholera vibrio, etc. They settle by preference on food, especially fruit, sweetstuff, cream and pastry. Harm may, therefore, ensue from eating this food in epidemic periods when there are swarms of flies.

Everything that can prevent flies obtaining a fresh supply of germs should be recommended, including disinfection and cleanliness of the patients, their linen, bedpans, slop-pails, sinks and latrines, on which cresyl and chloride of lime powder should be sprinkled. The water-closet system represents a considerable progress in the preventive hygiene of typhoid fever, by limiting the contagion by flies and the deposit of germs in pails or the subsoil.

War on the flies themselves and their reproductive activity is carried on by disinfection of the places where they lay their eggs by means of sulphate of copper, cresyl and chloride of lime, by clearing out dung-heaps, cleaning manure-pits, etc. It has been suggested that the dung-heap should be placed on hurdles slightly raised from the ground; the pupæ of flies which infest the bottom layer of the dung-heap will then fall upon the ground, where they are gobbled up by the poultry in country places.

The protection of the windows and doors of kitchens and dining-rooms with wire blinds, the employment of meat safes and wire covers over the food, constitute an extremely valuable *mechanical protection*. This simple and useful method cannot be too highly recommended in kitchens and canteens in association with the other prophylactic measures recommended in this work.

To destroy the flies *in situ* pyrethrum powder dusted at night on the shelves, furniture and tables will be of great service. Fly-papers, traps, special vessels, bird-lime, etc., may be used in houses, hospitals, infirmaries and ambulances.

Good results can be obtained by leaving at night, in the kitchen and places where flies accumulate, plates and saucers containing milk, or, better still, ordinary beer, to which formol (1 in 10) has been added.

These measures should be officially ordered in slaughter-houses, pigsties, porkbutchers' shops, butchers' shops, tinned meat factories, and generally in all establishments and factories concerned with food.

CHAPTER XV

PROPHYLAXIS OF TYPHOID FEVER IN THE ARMY

THE causes of typhoid fever are obviously the same in the army and in the civil population. The prophylactic measures already described find their application in a military environment. Owing, however, to its excessive susceptibility and almost uniform manner of life, food and age of its component parts, the army forms a special environment, in which prophylactic measures are perhaps more easily and readily carried out.

The creation of military bacteriological laboratories for the analysis of drinking-water, the cultivation of the blood and stools, the investigation of suspected cases and carriers; *the institution of the Chief Council for the Supervision of Drinking-water* intended for the army, which has rendered considerable service, the studies and reports to which the onset of epidemics at once gives rise with hygienic measures taken without delay, all testify to the important place taken by hygiene in our army.

The law of March 28, 1914 (Léon Labbé's law), makes anti-typhoid vaccination compulsory. Vaccination has been employed in certain French garrisons ever since the year 1911, first of all in East Morocco, then throughout the whole of Morocco, Algiers and Tunis. The appearance of formidable epidemics in certain garrisons, viz. at Avignon in 1912, at Montauban, Issoudun and Marseilles in 1913, and at Tours in 1914, determined at first the application and later the generalisation of this preventive method.

The description given in the general study of pro-

phylaxis will allow us to abridge our remarks in relation to prophylaxis in the army, both in war and peace time. Only a few supplementary details will be given.

As soon as an epidemic appears an attempt should be made to recognise and combat the initial cause, and to limit the extension of the outbreak. Consequently examination of the blood of patients and suspected persons should be made *as soon as possible* by the head of the district laboratory in time of peace, and by the bacteriologist of the army corps or army laboratory in war time.

After isolation and suitable cultures on special media, the most rigorous measures should be adopted as soon as the diagnosis is made. The patient is isolated in a special ward; in war time in a typhoid hospital. His stools, linen, bedpan and bath are disinfected in the way described below.

Removal to hospital must take place early. This should apply not only to undoubted cases, but also to incomplete forms, cases of gastric derangement and diarrhœa of a doubtful character.

The patient should be nursed by attendants who have been vaccinated against typhoid and paratyphoid, and are provided with a special set of clothes, which they should remove on leaving the ward. The attendants should wash their hands carefully after having bathed the patients, or changed their linen, or given them the bedpan or urinal. The use of rubber gloves is very useful, and considerably simplifies the precautions to be taken.

Typhoid cases suffering from secondary complications, such as streptococcal infection, pneumonia, diphtheria, etc., should be placed in isolation rooms, as such cases are undoubtedly contagious to other patients.

Soiled linen, bedclothes, handkerchiefs, drawers, etc., are steeped in buckets filled with warm water containing *Eau de Javelle* in the proportion of 20 per 1000. Linen thus treated can be handled without danger,

and does not allow any contagious particles to escape. Another method may be employed. The linen should be placed in a disinfecting bag consisting of strong and impermeable cloth, and the bags are then taken to the laundry. The high temperature of the washing soon gets the better of the typhoid bacillus.

Disinfection of the mattress and blankets is carried out in the incubator at 120° C. with steam to facilitate the penetration of heat.

The excreta are sterilised before being thrown away by means of a 5 per cent. solution of cresyl or a 5 per cent. solution of copper sulphate. The urinals, bed-pans and slop-pails, spittoons and their contents are also sprinkled with these antiseptic solutions and then scalded; water at 100° C. instantly kills the typhoid bacillus. Its bactericidal properties may be still more increased by adding 5 per cent. solution of carbonate of soda, which renders it alkaline and raises its boiling-point.

To disinfect woollen objects or clothes they should be treated with formol or formacetone vapour. Mattresses, pillows and bolsters require the same treatment, but they must be undone and the wool or horsehair exposed in thin layers to the action of these vapours.

One may also unpick and remove the covering of the mattress and plunge it in *Eau de Javelle* (20 in 1000) for twenty-four hours, and disinfect the wool and horsehair separately. But the use of the steam disinfectant is more practical.

Feather pillows and eiderdowns which cannot be sent to the disinfector should have their covering disinfected at the laundry and the feathers in formol vapour.

Spittoons should be treated with 5 per cent. solution of cresyl or a 2 per cent. solution of caustic soda.

Table utensils, such as spoons, plates, cups, etc., are collected in metal baskets of iron wire, and plunged for several minutes in boiling water rendered alkaline by a 5 per cent. solution of carbonate of soda.

Floors and walls contaminated by excreta or urine should be washed with a hot solution of 5 per cent. of caustic soda, or with *Eau de Javelle* of the same strength.

The installation of a drainage system in hospitals or wards greatly facilitates the emptying of the bed-pans and baths. When the baths have to be emptied by buckets after use a litre of *Eau de Javelle* should be poured into the bath, to disinfect at once the bath and its contents. The bath should not be emptied until some hours later.

We will now consider the prophylactic measures to be taken in barracks.

The cause of the epidemic having been determined, it should be combated without delay. It must not be forgotten that persons in the incubation stage of typhoid fever without any morbid symptoms disseminate the bacillus with their excreta in latrines. The water, if contaminated, should be boiled before use. It may be drunk after boiling, or as weak tea, if the barracks have no sterilising apparatus. If this is to be had, one must make sure that it is working properly, as examination has sometimes shown that it may be inadequate or imperfect. The rations must be supervised, and raw vegetables, strawberries and unboiled water prohibited.

If the epidemic originates in a town, the cafés, bars and restaurants must be put out of bounds, for the soldiers, who have wholesome water to drink in barracks, often contract the disease in such places.

The scale of work should be reduced.

After having sent the patients and suspected cases to hospital, and after having disinfected their sheets, bedclothes and body linen, the stretchers and ambulance wagon which have been contaminated by them should be disinfected if necessary. *An effort should be made to detect any abnormal forms of infection which may give rise to contagion.*

The doors and windows of kitchens, canteens and eating-rooms can be protected to advantage by a wire blind, to prevent the entrance of flies. Food

should be kept in a safe or under glass covers freed from flies. This *mechanical protection* against flies must be accompanied by the various precautions described in the last chapter relating to the destruction of flies, their eggs and larvæ.

We have already said that convalescents may have the typhoid bacillus in their fæces and urine. A search for carriers is possible only in peace time. Even then it does not yield all the results expected. Systematic disinfection of the latrines will serve to remove this cause of contagion if a drainage system does not exist. *One must on principle regard all excreta with suspicion.*

Carriers and, as an additional precaution, even those who have previously suffered from typhoid fever, should be forbidden any employment in connection with the kitchens, canteens, filters, or apparatus for sterilising water. Cooks should be ordered to wash their hands on their return from the latrines or the urinal.

During manœuvres all these measures are applicable. The same applies to *camps.*

Further, inquiry should be made of the municipal authorities about the sanitary state of the localities and villages in which the men will be quartered, and about any prevalent epidemics.

Specimens of water should be taken for rapid chemical and bacteriological examination (colimetry).

Inns and public-houses should receive special attention.

On the march passage through infected villages should be forbidden. If this measure cannot be taken, the medical officer must ask for absolute prohibition being given to the troops to stop at all in such places to buy any milk or drink (cider, etc.), or take any water.

In camps in which very severe epidemics of typhoid fever have often been observed very strict measures should be adopted to prevent the invasion and spread of the bacillus.

The camp should not be erected over a previously infected site or over old fæcal trenches. These must be looked for and avoided.

The kitchens and canteens should be situated far from the latrines, fæcal trenches, urinals and stables, owing to the danger of flies.

Whenever it is possible, especially in permanent camps, a drainage system should be provided.

The fæcal trenches should be carefully supervised, and disinfected with chloride of lime powder once a day in winter and twice daily in summer on account of the flies. Their approaches should also be powdered with antiseptics.

The water should be analysed and, if doubtful, sterilised.

Raw vegetables and unboiled milk may be the source of grave dangers, and should be forbidden as soon as suspected or definite cases of typhoid fever appear.

The occurrence of the first case requires immediate and energetic precautions, viz. dispatch of the patient to hospital, removal of the tent, incineration on the actual spot of the straw on which he lay, disinfection of linen, contaminated objects, etc.

Removal to hospital, into an observation ward for doubtful cases, containing patients with gastric derangement, etc., has a real practical importance. Their linen should be sent to be disinfected as if they were really suffering from typhoid fever, and the straw on which they lay should be burnt.

As many of these cases are due to infection by paratyphoid bacilli, Thiercelin's enterococcus, etc., these precautionary measures will always be advantageous.

Soldiers must be forbidden, on pain of severe penalties, to pollute with liquid human fæces the camp soil, the approaches to the tents and huts, and the surroundings of wells or springs.

Night latrines with pails should be installed as in barracks, being closed by day and carefully disinfected. They should be lighted up at night.

Protection of food against flies and the destruction of the flies themselves must receive special attention.

Kitchen refuse, scraps of food and rubbish should be burnt in special destructors, easy to construct and provided with a powerful draught. They should be situated at one of the extremities of the camp, so that the prevailing wind does not drive back the smoke upon the camp.

The specific prophylaxis of typhoid fever *in war time* is obviously based on the same principles as those set forth above.

The establishment of army and army corps bacteriological laboratories, as well as mobile sanitary sections with portable apparatus, forms part of the prophylactic measures required by the fight against typhoid fever in war time. They inform the Health Service as to the quality of the drinking-water, the exact nature of the diseases, as well as the doubtful cases, germ carriers, etc. They make blood-cultures, diagnoses of the first cases, which are always so important, and bacteriological analyses of drinking-water.

As the causes of epidemics are multiple, the prophylaxis of typhoid fever always presents the greatest difficulties in armies on active service. The specific preventive method, vaccination, alone enables us to combat them all successfully at once. We shall deal with this subject later.

War conditions do not always permit of every prophylactic measure being rigorously carried out. Medical officers will therefore need much energy, persistence, self-confidence and initiative to obtain results. But these results are always forthcoming when prophylaxis is applied conscientiously, without forgetting or failing to carry out even the minutest detail. Any neglect, omission or half-measures result in prolongation of epidemics and the death of a large number of soldiers. It is the duty of the medical officers whose mission it is to give the orders, as for those who have to carry them out, to neglect nothing

in the war against the germ of typhoid fever. It is a fact that soldiers in general are opposed to hygienic measures of any kind. These must, therefore, be made compulsory, and it must be realised that the rôle of the medical officer and hygienist, which is to keep a large body of men in a sound condition, is one of national defence. The commanding officer should be associated with these measures, and his assistance obtained by convincing him of their value.

All the prophylactic measures, therefore, which we have recommended find their application in war time. The bacteriological control of drinking-water, its purification by boiling or treatment with *Eau de Javelle*, should be carefully carried out. The chief medical officers and the divisional medical officer should exercise a constant supervision, so that *the men should not drink any other water than that which has been purified.* Every one knows that the soldier has a natural tendency to drink any water he finds, whether dangerous or not. It is not, therefore, enough to show him the grave risks he is running. He must be prevented from drinking such water by police measures, such as closing or guarding a suspected well or unwholesome spring.

The fight against flies which carry harmful germs forms part of the necessary prophylactic measures, and should be accompanied by the destruction by incineration of fæces, rubbish, kitchen refuse and putrescible matter, or by their disinfection by chloride of lime, cresyl, or 5 per cent. solution of sulphate of copper. The methods of protection against flies have already been described.

The fæcal matter of persons in the incubation stage and during the actual disease, and of convalescents and carriers as well, remains the essentially dangerous element of direct or indirect contagion.

It is to be found in large quantities in places occupied by troops. There can be no question of making a search for typhoid or paratyphoid carriers in a very large body of men. The German method, which is of

difficult application in peace time with the technique at present available, would be out of the question in war time. It is simpler and more practical, as well as more rational, *to consider on principle all human excreta as dangerous and to treat them as such.*

Dung-heaps keep up the supply of flies, which multiply in an extraordinary degree in war time. These dung-heaps often form enormous accumulations, and it is not without difficulty that the sanitary service of the army can rid the cantonments of them. If one cannot force the inhabitants to do away with dung-heaps, it is best to have them taken away by fatigue parties, and spread in thin layers over the cultivated fields in the neighbourhood at a distance from the houses.

Men with suspicious symptoms should be urged to report themselves to the medical officer without delay. It has too often been found that soldiers suffering from typhoid fever do not report sick until they have reached the last extremity and their strength is giving way. Some have been able to go to the trenches although they had undoubted symptoms of the disease. This reluctance on the part of the combatant soldier has very grave consequences, both for himself because it is the cause of the high case mortality observed in the present war, and for others because it results in specific contamination of the ground, trenches, drinking-water, etc., with excreta rich in bacilli.

The problem of contagion in the trenches undoubtedly raises considerable practical difficulties. The makeshift latrines erected in well-sheltered offshoots from the trenches are not always used by the soldier, either because he is in a hurry to relieve himself or because he has to change his position, which sometimes exposes him to the fire of the enemy. The deposit of fæcal matter in the trenches where the soldier fights, rests, takes his food, and, generally speaking, lives for several days, results in contaminating his clothes, boots and hands. This contamina-

tion is obviously followed by that of the alimentary canal. When mixed with mud the fæcal matter escapes notice, and is therefore all the more dangerous.

The occupation of the enemy's trenches after a fight offers the same grave dangers of contamination. This is the explanation of the propagation of typhoid and paratyphoid fevers, dysentery, enterococcus infections and trench diarrhœa during the present war.

For this reason regimental medical officers should endeavour to prevent, whenever possible, any fæcal contamination of the soil of the trenches. The offenders and the companies in which these cases of uncleanliness are observed should be regarded as responsible, and ordered to disinfect the areas contaminated by the excreta with chloride of lime. The disinfected matter should then be buried in deep holes far from the water supply.

Except under special circumstances, patients and doubtful cases should make only a very brief stay in the ambulances situated near the lines. They should be taken to special infectious hospitals, where there will be facilities for isolating them, for making bacteriological diagnosis by blood-culture, repeated if necessary, and for nursing them.

The removal of typhoid patients should be carried out under supervision. Sterilisation of the patients' fæces and urine during the journey should be ordered. Arrangements should be made to avoid contamination of the transport vehicles, automobiles, wagons, boats, canals, etc. There may be some risk in transporting to a distance typhoid patients who have reached an advanced stage of their disease, in whom intestinal perforation or accidents due to myocarditis are to be apprehended.

The official report should indicate without delay not only the definite and exact diagnosis, but also the possibility of suspected cases, so that precautions should be taken early to cut short the epidemic.

All the special precautions and measures we discussed in detail when we dealt with the prophylaxis of

typhoid fever in the civil population, as well as in barracks, camps and cantonments and during manœuvres. There is, therefore, no need to mention these again. In addition to supervision of the drinking-water, protection against flies, disinfection of fæcal matter, urine, rubbish, etc., we may remind our readers that every man who has had an attack of typhoid or paratyphoid, especially recently, should be forbidden to act as cook, as he may be dangerous in this employment.

It would be well if every soldier's book contained as an appendix a chapter on hygiene, informing him in a simple and summary manner how infectious diseases are contracted, especially typhoid fever, the precautions to be taken to avoid them,[1] the dangers of alcoholism, etc.

Specific prophylaxis does not apply to the infecting germ only, or merely aim at its destruction. It should also endeavour to protect from infection by *active* immunisation all the persons exposed to contract the disease. This active immunisation is obtained by inoculation of the dead virus. Such is the principle of *preventive vaccination*, which has given remarkable results whenever it has been properly carried out. We shall deal with it after our epidemiological study of paratyphoid fevers.

[1] H. Vincent, *Congrès International de Médecine.* Section de Pathologie Militaire. Paris, 1900.

CHAPTER XVI

ETIOLOGY AND PROPHYLAXIS OF PARATYPHOID FEVERS

Typhoid fever on the one hand, and paratyphoid fevers on the other, constitute entirely independent diseases. In spite of the close similarity of their symptoms, and although the bacilli causing them belong to the same family of micro-organisms, these affections do not confer upon each other reciprocal immunity. It may happen that the same person may contract in succession, and at a few months' interval, typhoid fever and then a paratyphoid fever. Cases have been known in which the three diseases, typhoid fever, paratyphoid fever A and paratyphoid fever B, have occurred within a little more than a year in the same person, who had been successively exposed to the contagia of these three diseases.

Such cases, undoubtedly, are not frequent. But one must consider the possibility of their occurrence in interpreting repeated attacks of typhoid fever in the same individual. Such cases are possible, but, in the absence of a blood-culture, an exact diagnosis cannot be made.

The nosological independence of paratyphoid fevers one from the other and from typhoid fever is also illustrated in epidemiology. Before the important discovery of paratyphoid bacilli by Achard and Bensaude in 1896, it is certain that the infections due to these pathogenic micro-organisms were usually confounded with typhoid fever, and sometimes with certain forms of cholera nostras. Bacteriological examinations, by indicating the exact nature of the infections and attributing them to their true pathogenic

agent, have helped to prove the existence of autonomous epidemics of paratyphoid fever. On other occasions cases of typhoid fever were found in association with paratyphoid fever. Before the war of 1914 paratyphoid fevers were seen in the form of small epidemics, usually of the B type. In the army, where, following the introduction of antityphoid vaccination, blood-cultures were taken from patients suffering from doubtful affections, this disease was found to be very frequent in soldiers, whether vaccinated or not. Some extremely violent epidemics which occurred at Marseilles, Avignon, Tours, etc., were exclusively due to the typhoid bacillus, and the local laboratories reported only a few isolated cases of paratyphoid fever B. Paratyphoid A was less frequent.

Sacquépée and Chevrel have noted that the town of Rennes was fairly often infected by paratyphoid fever. The disease is particularly frequent in parts of Paris and in the west of France (Brittany). It has been seen almost everywhere. In Europe, Germany forms the most important seat of paratyphoid A and B. This frequency of the disease, which may be so high as to constitute 10 per cent. of the diseases of a typhoid form, is doubtless connected with the nature of the food usually eaten in that country.

The existence of paratyphoid fevers has been noted in Italy, England, Holland, Roumania and other European centres; in Africa (Algeria, Tunis, Morocco, Libya, Egypt, Senegal, South Africa, etc.); in the United States, Brazil, Philippine Islands, Japan (Shibayama), Indo-China, etc. The disease is, therefore, ubiquitous.

War, by reason of the exceptional conditions which it creates, favours in the highest degree the appearance of gastro-intestinal disease, such as bacillary and amœbic dysentery, ordinary diarrhœa, and the so-called trench diarrhœa, as well as typhoid fever. The frequency of paratyphoid fevers A and B has thus been demonstrated, especially in August 1915, when they were predominant in the armies.

Vaccination against typhoid fever in no way predisposes to paratyphoid fevers A or B. Before the war with Germany these were extremely rare in the French Métropole army, although this contained more than 200,000 vaccinated persons. In the English army in India, which was almost entirely vaccinated against typhoid fever, there were only a few cases of paratyphoid fevers. It was the same in the United States army.

The war with Germany gave rise to a fairly large number of cases of paratyphoid fever through contagion (as well as of bacillary or amœbic dysentery), which were controlled by specific vaccination.

The influence of races and their predisposition to paratyphoid infection have not been settled. Cases appear to be more frequent in hot countries, but war, by greatly increasing the opportunities for contagion, is undoubtedly the most important of all favouring causes. Chevrel, on the ground that in a given country certain areas are specially affected, maintains that there are undetermined "regional influences." It is more probable that these influences are connected with defects in the hygiene of food, drink and housing.

Paratyphoid fevers are present in all seasons. But their curve is usually superimposed upon that of typhoid fever. It reaches its highest level in the months of August, September and October, *i.e.* during the hot period.

According to certain authors, the gravest forms are observed in winter.

All ages are susceptible, since young children, and even infants, may be attacked by paratyphoid as well as old men. The two sexes are affected in the same proportion.

Paratyphoid fever, either from its high contagiosity or as the result of ordinary conditions of infection, fairly often appears in small local or family epidemics, which may be very mild, or, on the contrary, severe. Its incubation period is generally from nine to fifteen days.

Etiology of Paratyphoid Fevers.

The chief causes of paratyphoid fevers A and B are the same as those of typhoid fever.

The paratyphoid bacilli gain entrance to the organism by the alimentary canal, reach the blood (where they are found on cultivation), and multiply in the lymphoid organs, spleen, bone-marrow, viscera, gall-bladder, etc. The bacilli are to be found in the blood during the first few days of the disease, but as a rule they stay there a shorter time than the typhoid bacillus. They are discharged in large quantities, and in a much more continuous and regular manner than the typhoid bacilli, in the excreta and urine. The mechanism of their elimination, however, is the same.

As in typhoid fever, paratyphoid bacilli may persist for very long after recovery, either in the fæces or urine. *Temporary* or *chronic* paratyphoid bacillus carriers are found who constitute, with the patients themselves, the disseminating agents of pathogenic bacilli.

The average proportion of carriers among those who have had paratyphoid fever is 4 per cent.

Paratyphoid bacilli are transmitted by the excreta, urine, pus and bronchial secretions, either directly by the patient or carrier to the healthy subject, or indirectly, intermediaries being very numerous, as in the case of the typhoid bacillus.

As our account of the propagation of typhoid fever applies to paratyphoid fever A and B, the present description may be curtailed.

Fæcal matter is the most dangerous of all the elements of contagion. This is why direct contagion fairly often affects nurses, visitors and patients in the next bed who do anything for them, as the hands are the most usual means of conveyance. They become contaminated when the patients are being attended to, *e.g.* when they are given a bedpan or have their linen changed.

In like manner, by depositing their excreta on the ground, or near springs and wells, or vegetable gardens,

etc., temporary or chronic carriers contaminate them, and may be the starting-point of epidemics of uncertain origin. In the case of carriers employed as cooks, the absence of cleanliness and neglect to wash the hands are equally important causes of infection in families, restaurants and houses, barracks, schools, refuges, asylums, etc.

The spread of contagion by food is certainly very frequent. But, unlike the typhoid bacillus, which is always transmitted in such cases by food which is secondarily affected and is incapable of infecting animals, *paratyphoid bacilli may readily multiply in animals*, giving rise to diseases the nature of which is not always suspected, and which are for that reason all the more dangerous.

Unlike typhoid fever, which is an exclusively human disease, paratyphoid infections or Salmonelloses, may affect both man and animals, and be transmitted from the former to the latter and vice versa.

According to Morgan, Mori, and Gardenghi, the alimentary canal of domestic animals (dog, cat, rabbit, pig, etc.) may contain paratyphoid bacilli, and therefore the fæcal matter of animals, as well as human excreta, may serve as the means of conveying the paratyphoid A or B bacillus.

So, if this observation is correct, animals may become actual carriers of paratyphoid organisms.

On the other hand, the pig, ox, cow, calf, and much less frequently the sheep (Babes) and the horse, may be infected by bacilli belonging to the group of Salmonelloses, which includes closely related micro-organisms, especially *B. enteritidis*, which is most frequently found in food-poisoning. This bacillus causes in animals a rapidly fatal septicæmia, infective gastro-enteritis with profuse diarrhœa (in the calf), arthritis, metritis (in the cow), and closely resembles the paratyphoid B bacillus. Its pathogenic characters and reaction on sugar media are the same. Experimental or human serum, however, which agglutinates one of these micro-organisms, does not definitely agglutinate the other.

There is, therefore, a reason for separating them, especially as the symptoms which they cause in man are somewhat different.

Direct contagion by paratyphoid bacilli is, therefore, liable to be transmitted not only from man to man under the same conditions as the typhoid bacillus, but also from diseased or healthy animals (carriers) to man, and doubtless vice versa.

The factors of indirect contagion are necessarily also at work in the propagation of paratyphoid bacilli. They act more frequently than in typhoid fever, *because paratyphoid A and B bacilli are much more resistant than the typhoid bacillus to external causes of destruction.* They are more long-lived than the typhoid bacillus. They may persist longer in water and putrefying media like meat, in which the typhoid bacillus does not survive.

Drinking-water has frequently been accused of conveying the paratyphoid bacillus. Examples have been given by Sacquépée and Chevrel, and by Darde. Chevrel recorded in his thesis a mild epidemic of twenty-five cases of paratyphoid fever B which occurred after drinking the water from a cistern.

The injurious effect of drinking-water has been proved at Rennes, as well as in Germany, Austria, the United States, etc.

The use of impure cider prepared with contaminated water was incriminated in an epidemic which attacked the 35th artillery regiment in 1908, and gave rise to fifty-four cases (Follin and Fortineau).

In most of these epidemics the paratyphoid B bacillus was concerned.

Meat is still more frequently the starting-point for infections due to paratyphoid bacilli. These food infections, of which Polin and Labit and Sacquépée have given a very complete description, have sometimes a sudden and almost immediate onset, with symptoms of acute gastro-enteritis which may simulate cholera, and sometimes, on the contrary, a normal incubation with a more typical course. The immediate onset

of symptoms has been attributed to intoxication by thermostabile poisons developed in putrefying meat or coming from diseased animals: it has also been thought that putrefying meat contained toxic nitrites which might cause these rapid symptoms.

The later infective symptoms are due to infection by the paratyphoid bacillus, Gærtner's bacillus, or another representative of the group of Salmonelloses.

The contagious character of meat is explained by what we have said with regard to the latency of the paratyphoid B bacillus in the pig's intestine. In Germany bacilli belonging to the group of Salmonelloses are extremely common in pigs' intestines: 7 per cent. of the animals contain them, and sausages made with pigs' meat are also infected with the paratyphoid B bacillus.

It is in Germany, therefore, that the largest number of epidemic cases of paratyphoid fever have been seen following the ingestion of meat from diseased animals.

The possibility of infection can only be allowed when the meat (pork, beef, or veal) has been insufficiently cooked. According to Vallin, the central temperature of roast meat does not often exceed 45–50° C.; in hams weighing 5 kilogrammes the central temperature does not reach 60° C. after three hours' cooking. Now, typhoid bacilli are killed only at a minimum temperature of 57–58° C. prolonged for an hour. When infected food is given raw or half cooked to animals such as a monkey (van Ermengem), dog, mouse, guinea-pig or rabbit, a similar infection may result.

The remarkable power of resistance of typhoid bacilli explains how it is that after the death of the infected pig, ox or calf, *the bacillus continues to multiply rapidly*, especially in summer time, in pieces of meat, and also to secrete abundant toxines whose presence explains the symptoms which appear almost immediately. In this respect investigations made with *B. enteritidis* are conclusive. Persons who, under the impression that it was wholesome, partook of the

meat of some animals inoculated with the bacillus of the Morseele epidemic, were all attacked with gastro-enteritis. When kept in the ice-chest, the meat of these animals is, for this reason, much less dangerous.

The consumption of pork-butchers' meat, galantine (Netter), meat pies, black puddings, sausages of any kind, etc., has been the occasion of numerous cases of paratyphoid B fever. Further, as we have already said, it has frequently been possible to isolate the paratyphoid bacillus, by cultivation, from the inside of sausages or pies made with minced meat, or brawn. Organisms so isolated, in spite of their presenting the characters of paratyphoid bacilli, are not always pathogenic to the animals who are made to swallow them. Perhaps in such cases their virulence has disappeared or become attenuated.

It appears certain that when fresh meat gives rise to a large epidemic, the meat, which had been consumed shortly after slaughtering, came from diseased animals infected by the bacillus. In a total of fifty-one epidemics of Salmonelloses, Sacquépée found that nine were due to pork, seven to veal, and seven to beef. The meat of diseased poultry has sometimes been incriminated.

Leaving aside, however, the infections due to *B. enteritidis*, which are more common, but which, perhaps, should not be considered strictly as paratyphoid infections, it is none the less certain that paratyphoid bacilli may be transmitted by meat which is uncooked or is insufficiently sterilised by cooking. Meat pies, pork-butchers' meat, etc., may have themselves been contaminated secondarily, when they were being prepared in the kitchen, by a carrier's unclean hands; by contaminated instruments, vessels or tables; by the numerous flies which convey the micro-organism; by ice, etc.

In other cases the paratyphoid bacillus may be present in the intestine of the animal itself, and contaminate the sound meat when the carcase is being cut up. When the external temperature is high, the

bacilli also find a satisfactory culture-medium, and may multiply with extraordinary rapidity in mince, saveloys, sausages, pies, etc., all the more so as they are facultative anaerobes. This is the explanation of infections following the consumption of these foods. Preserved pork, ham (Pottevin), corned beef, dried goat's meat, sausages and *pâtés de foie gras*, galantine, etc., have given rise to such cases.

Contamination by hands, flies, ice and tables or vessels which have been used for infected food or meat furnishes an explanation of the cases of paratyphoid fever or fever due to *B. enteritidis* occurring after consumption of fish, semolina, vermicelli, cakes, beans, etc. Cream has also given rise to similar digestive disturbances. But in that case the micro-organism may have been brought by the milk.

Cases of epidemic paratyphoid fever are on record following the use of milk (unboiled). Max Levine and Fred. Eberson have related a similar case in the College of Ames, Iowa. The milk had been contaminated by the hands of a carrier or a convalescent who had been milking cows and bottling the milk.

Oysters, mussels, cockles, and other shell-fish are an equally frequent cause of paratyphoid contagion. Cases of this disease due to consumption of ordinary oysters, or so-called Portugal oysters, appear to be becoming more frequent, owing to the deplorable habit of those who own or lay oyster beds of keeping them in harbours, in water infected by fæcal matter and sewer-water.

Prophylaxis of Paratyphoid Fevers

The prophylactic measures relating to paratyphoid fevers A and B are identical with those of typhoid fever properly so called, but they also demand a special hygienic supervision of slaughtered meat, of insufficiently sterilised and preserved meats, vegetables and fish, as well as of all forms of pork-butchers' meat, because infection may be spread by the meat of diseased

animals, or their excreta, or the fæces of domestic animals who may be actual carriers of the paratyphoid B bacillus.

In the civil population, as in the army, complete cooking or effective sterilisation of preserved food of all kinds, prevents this special mode of contagion by destroying the paratyphoid bacilli, which are killed at 60° C. Milk ought not to be taken until it has been boiled. Lastly, food of any kind, whether sterilised or not, may become a cause of contagion, through being handled by carriers or exposed to contagion by flies. It is important, therefore, to find the carriers and to remove them from any culinary employment in boarding-houses, hospitals, asylums, etc., as well as in the army, both in peace and war time (kitchen, canteens). It will be wise to examine the stools of those who have had a paratyphoid fever before giving them employment of this kind. Persons who suffer from chronic hepatic or biliary lesions, such as jaundice or gallstones, are often open to suspicion; useful information can be obtained by examination of their stools.

We will not dwell any longer on the prophylaxis of paratyphoid fevers, but will refer our readers to what we have said in the chapter devoted to the prophylaxis of typhoid fever.

To facilitate this prophylaxis the notification of paratyphoid fevers should be made compulsory.

For paratyphoid fevers A and B, as for typhoid fever, vaccination constitutes the best prophylactic measure.

CHAPTER XVII

ANTITYPHOID AND ANTIPARATYPHOID VACCINATION

The prophylaxis ot typhoid and paratyphoid fevers has been most successfully completed by active immunisation against these infectious diseases. It may be said that considerable progress occurred as soon as this preventive method was introduced into practice in the civil population and the army. Numerous articles, to which there is no need to allude, have appeared on this subject.

Human vaccination was preceded by an experimental period. The principle of immunisation by living or dead cultures or their soluble products was established by Pasteur in the case of anthrax and fowl-cholera, and has since been extended by a large number of scientists to anthrax (Toussaint, Chauveau), symptomatic anthrax (Arloing, Cornevin and Thomas), the bacillus of malignant œdema (Roux and Chamberland), the bacillus pyocyaneus (Bouchard and Charrin), the bacillus of hog cholera (Theobald Smith, Salmon), etc., and lastly, in 1888 and 1892, to the typhoid bacillus by cultures heated to a temperature of 120 or 100° C. by Chantemesse and Widal, and to 50° C. by Bruschettini (1892), etc. Most of these authors used heat to kill the virus. T. Smith and Salmon, as long ago as 1886, immunised animals against hog cholera by several injections of cultures heated to 58° C., a temperature which did not impair the vaccine. The vaccination of man against typhoid fever is consequently due to Pasteurian methods.

Almost at the same period, *i.e.* in 1896, Pfeiffer and Kolle on the one hand, and A. E. Wright on the other,

applied to man vaccination against typhoid fever by heated cultures. As a matter of fact, it is the English scientist, A. E. Wright, who is the true initiator of this method in man rather than Pfeiffer and Kolle, who made no extensive use of the method, whereas A. E. Wright applied it in the English Army to a large number of individuals with very successful results.

Wright first of all made use of broth cultures ten to twelve days old, sterilised at 60° C. with the addition of 0·5 per cent. of lysol. Subsequently the duration of the cultures was reduced to forty-eight hours, and the temperature of sterilisation to 53° C. (Leishman).

But the bacillus was not quite killed at this temperature; the addition of lysol finally destroyed it. Three injections were made, the first consisting of 500 million bacilli, the second 1000 millions, and the third of 1500 millions.

After the publication in London of the *Report of the Antityphoid Committee*, according to which cultures heated above 65° C. lose their immunising efficacy, the sterilisation has been carried out at a lower temperature.

The vaccine employed in the United States since 1909 is that of Russell, prepared in the laboratory of the Army Medical School.

The bacilli are grown on agar for twenty hours, washed off with normal saline solution and then killed by heating to 55–56° C. for seventy-five minutes. A solution of 1 in 100 tricresol is then added. The vaccine contains 1000 million bacilli per c.c. It is employed in the American Army and Navy.

The vaccine prepared by Chantemesse is made in the same way as in the United States, 0·25 per cent. of cresol being added. It is used in the French Navy. Four injections are given. The doses injected are 0·25 c.c., 0·50 c.c., 0·75 c.c. and 1 c.c.

Le Moignic and Pinoy have recommended a vaccine made with killed bacilli suspended in sterilised oil.

Renaud has proposed a vaccine which has been exposed for thirty minutes to the rays of a quartz lamp.

Lumière and Chevrotier have proposed a dried and pulverised mixture of typhoid bacilli, B. coli and paratyphoid bacilli killed by heat. The powder is made up into keratinised pills which are swallowed.

Castellani was the first to attempt vaccination with living cultures; 310 persons were given cultures which were first attenuated at a temperature of 50° C., and then normal ones. Three or more injections were given. Nicolle, of Tunis, also used living cultures which had undergone two washings, the first a complete, and the second an incomplete one; the turbid supernatant fluid containing 14 million bacilli per c.c. Intravenous injections of this vaccine are given, the first containing 400 millions, the second 1200 millions.

Besredka's method is founded on the use of a living sensitised vaccine. The typhoid bacillus is cultivated for forty-eight hours on agar, washed in saline, and then treated with antityphoid serum. After remaining in contact with it for twenty-four hours, the living bacilli are decanted and washed and emulsified in normal saline. This vaccine contains 1000 million bacilli per c.c.: 1 c.c. is first injected, and then 2 c.c.

The use of living vaccines does not appear to have become general. The objections to it are (1) the possibility of those using it contracting typhoid fever, (2) of overworked or enfeebled subjects becoming infected with an immediate or delayed growth of the bacillus in their biliary passages, (3) the creation of carriers. The employment of a dead virus has therefore been more generally adopted.

It is possible to kill the typhoid bacillus by other means than heat, especially antiseptics. We have, in fact, seen that the vaccine of Wright and Leishman is much attenuated by a temperature of 53° C. and is killed by lysol. Semple has recommended carbolic acid (5 per 1000) which has recently been employed in the Italian army.

Ranque and Senez have proposed the employment of a vaccine sterilised by iodine, which has been in use especially at Marseilles.

The use of a vaccine sterilised by ether (H. Vincent) is founded on the principle that the typhoid bacillus and micro-organisms belonging to the same group are very sensitive to the action of ether. The typhoid bacillus is killed by ether in thirty-five or forty minutes on the average. Ether also possesses the advantage of removing the fatty substances which are present in large quantities in the protoplasm of the bacilli and serve to make the vaccine painful and fever-producing.

Vincent's vaccine is made of ten strains of typhoid bacilli of different origin, which makes it polyvalent. Strains of paratyphoid bacilli A and B have been associated with them from the first, *i. e.* since 1910 (*triple* vaccine).

The antityphoid vaccine as first used in the army was inoculated in successive doses of 0·5 c.c., 1 c.c., 1·5 c.c. and 2 c.c., but the number of injections was first reduced to three and then to two. Thus, in 1913, 26,000 soldiers were vaccinated with three injections each, in the XIVth legion with excellent preventive results. The total number of bacilli injected has varied from 1600 to 1800 millions.

Lastly, there has long been a question as to whether antityphoid vaccination could not be simplified under war conditions. In the Official Report presented in April 1914 to the Committee of the *International Health Office*, H. Vincent concluded that under these circumstances a modified vaccination consisting of only two injections of antityphoid vaccine should be performed with somewhat stronger doses ; the immunity thus conferred being obviously less powerful and less prolonged.

This method was proposed and carried out at the beginning of the war, and in 1915 in the French army at the Front. The English army have also used it with heated vaccine, repeating the injections at the end of a year.

What is the quantity of vaccine needed to confer immunity, and what is the duration of this immunity ? As a matter of fact, *the immunity and its duration are in direct relation* not to the number of the injections, nor even, properly speaking, to the quantity of vaccine

injected, but *to the number of typhoid bacilli inoculated.* The degree of virulence of the bacilli has no influence. The technique of preparing the vaccines should not aim at acting violently on the bacilli. Any pronounced modification, whether natural or artificial, of the micro-organisms weakens or destroys their powers of producing immunity, *e. g*, a temperature above 60° C., certain antiseptics, oxidising agents, etc.

A dose of 500 to 1000 million typhoid or paratyphoid bacilli killed by ether confers a considerable immunity, or considerably attenuates the gravity of the injection. The number of cases of typhoid fever which may occur during the year following an injection of 1300–1500 million bacilli killed by ether is 0·50 per 1000 on the average in a highly infected population. The duration of the immunity conferred by this dose is from one to two years on the average. The immunity may be affected by the degree of enfeeblement or overwork of the individuals who have been exposed to contagion.

The minimal protecting dose of antigen is between 1300 and 2000 million typhoid bacilli. With a dose of 3000 millions experience has shown that the proportion of cases of typhoid fever in the vaccinated who have been very much exposed to contagion is about 0·25–0·35 per 1000. The injection of 4000–5000 million bacilli killed by heat considerably reduces the susceptibility, even in soldiers who are engaged in fighting and are suffering from exhaustion. One frequently meets with a series of 20,000 vaccinated soldiers and more who have been exposed to contagion, *and do not show a single case of typhoid fever.*

The duration of the immunity resulting from the inoculation of 3000–5000 million of typhoid bacilli killed by ether exceeds four years, according to experience in Morocco, and it is very probable that in many of those who have been vaccinated in this way it may persist throughout life, thus resembling the immunity conferred by an attack of typhoid fever.

What we have called the "protecting dose" is weaker in the case of the paratyphoid bacilli A and B

than in that of the typhoid bacillus. Considerable immunity is obtained by 1000 and still more so by 1500 million of paratyphoid bacilli killed by ether.

It is obvious, therefore, that there is no need to inject excessive quantities of antigen to obtain protection against typhoid and paratyphoid fevers.

Mixed Vaccination.

The nature of the vaccination should obviously depend on that of the epidemic diseases which one has to fight. In epidemics in which typhoid fever is the only disease, antityphoid vaccine is used.

The co-existence of paratyphoid fevers in the same community which has been exposed to contagion should entail the use of a mixed vaccine or the successive injections of different vaccines. Both methods have been employed in the French army with similar results.

Castellani has vaccinated a certain number of persons against typhoid and paratyphoid fevers, and also against dysentery or cholera simultaneously by means of mixed vaccines.

It is, however, the double vaccine antiparatyphoid A and B or the triple vaccine antityphoid and antiparatyphoid A and B, which are most commonly employed.

The triple vaccine designated by the name of T.A.B. vaccine (ether vaccine) was first employed in the French army in 1910–1911. The same mixed vaccine was used in 1911 at the time of the first official application of vaccination in East Morocco. Some was sent in 1912 for use in the sections of the hospital orderlies, as well as in several garrisons of the Métropole army at Casablanca and Oudjda. Vaccination with the triple vaccine, or T.A.B., was repeated in East Morocco in 1913 and 1914. Since October 1914 the triple ether vaccine has also been used on a large scale by E. Sergent and L. Nègre, more than 100,000 men being vaccinated among the troops stationed in Algeria.

Its use has become more extensive since statistics have shown the relative frequency of paratyphoid fevers

among the armies fighting at the Front in the present war.

Lastly, the same triple vaccine, or T.A.B., sterilised by ether and prepared at the Institute of Milan, was employed in 1912 and 1913 among the Italian troops fighting in Libya and Cyrenaica, as well as in the garrison of Brescia and at Careno (F. di Cavellerleone, Santoliquido) with the most striking results.

Ever since the year 1911, successive attempts have been made in the French army, with varying proportions of typhoid and paratyphoid bacilli, to determine the best composition of the triple vaccine, that is to say, the one which combines the minimum reaction with the maximum immunity.

The mixed vaccine first employed in the French army contains 500 millions of typhoid bacilli per c.c. plus 250 millions each of paratyphoid bacilli A and B. Vaccination at present is performed with two injections of a vaccine containing per c.c. 1000 million typhoid bacilli and 500 millions of each of the paratyphoid bacilli.

Experience has shown that a more concentrated form of this ether vaccine may be used without causing more numerous reactions. A *single* injection of a larger dose may be given. The quantitative estimation of the bacilli is made at the Army Laboratory for the various vaccines, typhoid, paratyphoid A and B, or T.A.B., by means of the opacity-meter with rays selected by Vles,[1] tutor at the laboratory.

[1] The principle of this apparatus is as follows. Two luminous circuits derived from the same source traverse, one the vaccine to be tested, and the other an absorbing system (polarisation system) by means of which one can vary the intensity of the circuit. The rays traverse a coloured screen which allows only the red-orange light (λ 615) to pass. The rays constituting the two circuits form two juxtaposed images in the eye-piece of the same glass. The equalisation of the two portions of the field is established as in a photometer, and the graduation is read off. The latter, which depends upon the absorbing system, indicates the amount of bacteria in the vaccine examined, owing to the previous standardisation. This apparatus also allows one to determine what solution should be made in the stock emulsion of bacilli to obtain a vaccine with 100,000 bacteria per c.c.

This apparatus is exactly standardised against emulsions of bacilli in suspension in normal saline solution, whose quantity of bacilli has been determined by a previous count.

The Army Laboratory also prepares antiparatyphoid A or B vaccines, and mixed vaccines A and B, the former containing 500 millions and the latter 1000 millions (500 millions of each bacillus).[1]

In addition to the simple antityphoid vaccine Chantemesse and Widal also employ the triple heated vaccine (antityphoid and antiparatyphoid A and B), which contains 1500 million bacilli per c.c. Four injections are given with the following doses, 1 c.c., 1·5 c.c., 2 c.c., 3 c.c. When circumstances require it, three injections are given in doses of 1·25 c.c., 2 c.c., and 2·5 c.c. The triple heated vaccine, No. 2, is injected twice in doses of 1 c.c. and 2 c.c. respectively. It contains 3,300,000,000 bacilli or 1100 millions of each of the typhoid and paratyphoid bacilli.

The lipo-vaccine of Le Moignic and Pinoy contains 3000 million bacilli per c.c. One injection only is required.

The technique of injecting the vaccine is the same for all vaccines except as regards the region chosen. The injection is given subcutaneously, not intra-muscularly, either in the subclavicular region, or on the outer aspect of the deltoid area, or behind the spine of the scapula. The last site has been chosen because it is less rich in nerves and vessels, as the vaccine may sometimes penetrate a vessel and then give rise to an almost immediate febrile reaction.

Injections should be carried out aseptically. One should make certain that the ampullæ are hermetically sealed, as some of them may have been cracked in transit.

[1] It is important to know that certain glasses have a considerable alkaline reaction (0·010–0·018 per litre in NaOH). Vaccine prepared or kept in vessels or ampoules made of this glass undergo bacteriolysis and becomes much clearer. It has, nevertheless, a normal bacterial content.

Persons who have been vaccinated should be in a state of repose. Fatigue preceding or following the injection of vaccine is, indeed, an important cause of post-vaccinal fever. It is also accompanied itself by a temperature of 100·4° F. or more apart from any vaccination. It has therefore been found that vaccination of soldiers at the Front during the war sometimes causes much more numerous febrile reactions than behind the lines. These reactions are most pronounced in men who have come back from the trenches. On the other hand, *after a rest of several days*, they become very rare.

It has fairly often happened that soldiers who have been vaccinated have had to fight a few hours after the injection, without any complications developing.

In some foreign armies the men go to bed after they have been vaccinated. This practice obviously diminishes considerably the proportion of cases with vaccinal fever.

Another important precaution consists in making them take only a light meal (tea or soup) on the day of injection. Persons who have eaten to excess may suffer from vomiting or diarrhœa, in other words, from an attack of indigestion which it is consequently possible to avoid.

During the cold season precautions should be taken to prevent the soldiers catching a chill during vaccination. They should not therefore be undressed a long time in advance, and they should wait in a warm room. In vaccinated persons who suffer from pain in the limbs and fever, aspirin in doses of 50 cgm. soon causes relief. As is well known, this drug may produce skin eruptions, more rarely fainting attacks, or transitory anuria in predisposed subjects. Antipyrine should not be given, as it is a more frequent cause of these symptoms.

The commonest causes of a febrile reaction following injection of vaccine are as follows: (1) Fatigue or over-work; (2) Acute alcoholism; (3) Too large a

meal; (4) *Any acute concurrent diseases*, and certain chronic diseases, from sore throat to typhoid fever or paratyphoid fever, malaria, influenza, tuberculosis, etc.; (5) Lastly, but not invariably, a recent attack of typhoid fever, whether unrecognised or not.

It is well to insist on the reaction which occurs when vaccination is performed on persons who are in the *incubation stage* of typhoid fever or paratyphoid fever, or at the onset of these diseases or suffering from an ambulatory attack. The fever which appears then is analogous to that which is caused by the injection of tuberculin in the tuberculous, or of mallein in those suffering from glanders. In war-time when typhoid diseases are so common in the non-vaccinated, it is important to be familiar with all those causes which determine fever,[1] so as to refuse or postpone vaccination and to give the reactions observed their true interpretation.

A large number of reactions seen at the Front are due to the vaccination of persons who are already invaded by typhoid or paratyphoid bacilli. It may also be noted that many subjects who have been vaccinated during the incubation period, escape typhoid or paratyphoid fever, thanks to the injections, having acquired immunity before the period of general infection.

Accurate observations made during severe epidemics like those at Avignon, Tours, etc., have shown that when the vaccination is performed at the beginning, or even in the middle of the incubation period, the subject has a good chance of escaping typhoid fever.

[1] Some medical officers who had observed vaccinal fevers during an epidemic, thought of taking the temperatures of the soldiers to be vaccinated *before* giving the injections, during epidemics of typhoid, paratyphoid, influenza, or an eruptive fever. The thermometer showed that a large number of men were feverish and were already suffering from one or other of these diseases (Rouget, Tournade, etc.). Identical observances have been made during epidemics of influenza. *We have thus an explanation of a large number of febrile reactions*, which are not caused but increased or brought to light by the vaccine.

By taking the simple precautions which we have just described, the number of febrile and other reactions following vaccination is considerably restricted.

Consequently the actual number of definite contra-indications to the use of vaccination is limited.

In this description which deals exclusively with the practical side of the question, it is necessary to state exactly what these contra-indications are.

Some are *temporary*, others are *permanent*. The former have only a secondary importance, since they mean merely a postponement of the injection. It is best, therefore, to make a summary medical examination of the subject to be vaccinated, and if he is ill or worn out, to put him off till the following week. This procedure enables the indisposition or acute disease either to disappear or to show itself in its true colours. This simple precaution very often saves the doctor injecting a patient who might be suffering on the same day from an acute infection, such as pneumonia, meningitis, or an eruptive fever, with a grave prognosis, the explanation of which, as has sometimes been found, is too far removed from the truth.

It also considerably reduces the frequency of cases of fever by exclusion from vaccination of persons with slight affections, bronchitis, sore throat, etc.

Permanent contra-indications are the same in all countries and all armies (Wright), viz. severe organic disease, tuberculosis, chronic pleurisy, with or without thoracic deformity, arterio-sclerosis and aortitis, myocarditis, non-compensated endocarditis, diabetes, chronic nephritis with signs of renal insufficiency, hæmaturia, etc.

Malaria is by no means a contra-indication, with the exception of acute cases or malarial anæmia or cachexia. In Algeria, Tunis, Morocco, Salonica and the Belgian Congo, where malaria is very frequent, vaccination is in general use among the troops.

The only precaution consists in making the men with chronic malaria undergo a quinine cure and giving them 75 cgm. or 1 gramme of quinine on the day

preceding and on the actual day of the injection. Experience has shown the possibility of a return of a malarial attack when this precaution is neglected.

There is no harm in vaccinating syphilitic subjects. When they present active lesions one should wait until they clear up before performing vaccination. In some cases one may be at a loss to know whether vaccination should be performed. *A trial injection* should be given of ½ c.c. of antityphoid or antiparatyphoid vaccine, or 1 c.c. of the T.A.B. vaccine. The temperature should be taken two hours later and on the next morning. If there is a violent reaction one should postpone the case or else vaccinate with small fractional doses. This trial injection will be of great service.

The vaccination of subjects who are delicate but without any visceral lesions is quite feasible. It is very often found that they tolerate injections of vaccine without any reaction.

Recourse, moreover, may be had to the fractional method of giving weaker and more frequent doses, *e. g.* 0·75 c.c., when the case is not urgent. The total number of bacilli to be injected must, however, be given.

Tuberculous cases in which the process is stationary and not an open one, may be vaccinated if the general state is satisfactory, care being taken to put them to bed on the day of each injection.

It has been said that antityphoid vaccination predisposes to tuberculosis and pleurisy, but this does not appear to be the case.

On the one hand, tuberculosis is much rarer in soldiers in Algeria, where typhoid fever is frequent, than in France, where the latter disease is much less widely spread. On the other hand, it has not been found that a larger number of cases with acute or chronic tuberculosis occur among vaccinated than among non-vaccinated soldiers. This observation has often been made in the present war.

Vaccination against typhoid fever does not cause any predisposition to paratyphoid fevers, scarlatina, measles, cerebro-spinal meningitis, etc.

Cardiac cases with compensation may be given the benefit of vaccination by performing it in the manner already described by means of small and more numerous doses. It has also been performed with ordinary doses (H. Vincent, Bardot and Ledoux-Lebard, etc.). But it should not be done in the case of patients suffering from lesions of the aortic orifice, aneurysms, or those suffering from œdema, dyspnœa, etc.

Patients with myocarditis should not be vaccinated. This affection should be sought for in those who have previously had an infectious disease, such as diphtheria, pneumonia, broncho-pneumonia, typhoid fever, etc.

With these exceptions it may be maintained that the great majority of persons may be vaccinated without any harm.

Even advanced age is not a contra-indication, but diseases or lesions of the viscera and arteries may be an objection to vaccination.

Subjects of fifty-five or sixty years of age have been vaccinated before leaving for Morocco. At the Front when certain villages in the Argonne had been invaded by typhoid fever, the children and the youngest inhabitants were vaccinated. As typhoid fever then appeared exclusively among the aged, they were inoculated also, though they were sixty to seventy years of age, without any special incident occurring (Combe).

After having vaccinated albuminuric cases without finding any aggravation of their condition or fever in consequence, we recommended at the beginning of 1916 that young men with albuminuria should be vaccinated when they had no symptom of renal insufficiency. Observations in a certain number of depots (Paris, Versailles, Issoudun, Perigueux, Libourne, etc.), on vaccination with the triple vaccine or T.A.B., showed that not only did the frequency of albuminuria not increase or even keep at the same level, but that it actually diminished in 80 per cent. of the cases consisting of young men with varying degrees of albumin (from mere traces up to 0·50 gramme or 1 gramme of albumin).

Among 141 albuminuric cases who had received four injections of T.A.B. vaccine, examination of the urine made from a week to a fortnight after the last injection by the regimental medical officers or dispensers showed that albuminuria persisted in only twenty-one. Vaccinations of this kind were made in a large number of other cases of albuminuria with similar results (Peyrot, Fratelli, etc.).

It is obvious, therefore, that T.A.B. or typhoid vaccine has no effect upon the normal kidney. Some cases of paroxysmal hæmoglobinuria received the four injections. In Morocco German prisoners who had previously had bilious hæmoglobinuric fever were vaccinated without ill effect. Cases of nephritis, however, with œdema or symptoms of renal insufficiency and uræmia, as well as those who present symptoms of hypertension associated with cirrhotic kidney, should not be vaccinated.

Widal and Méry have vaccinated patients in hospital with albuminuria who showed none of the severe functional disturbances of Bright's disease. Some had had œdema, and one had had 11 grammes of albumin in the urine. Inoculation with heated vaccine was made under favourable conditions, *i. e.* in hospital, and while the patients were enjoying complete rest, circumstances which, it is true, do not occur in military practice. Vaccination did not cause a return of the œdema nor an increase in the nitrogenous retention. One of the patients had a return of hæmaturia four days after each of the two injections.

Widal and Méry conclude that every case should be postponed in which there is a recent history of hæmaturia or acute nephritis, or in which there has been more than a gramme of albumin per litre or more than 0·50 centigramme of urea per litre of blood serum.

We have already given the doses of heated vaccine and sensitised vaccine which should be employed. The doses of the ether vaccine for the adult are as follows—

1. Vaccine T (*antityphoid*), containing 500 million bacilli per c.c.

Complete vaccination { 1st injection 1 c.c.; 2nd „ 1½ „; 3rd „ 2 „

or if *reduced* vaccination in two injections is performed—

Reduced vaccination { 1st injection 1 c.c.; 2nd „ 2 „

In less vigorous subjects these last two doses should be smaller, viz. 0·75 c.c. for the first, and 1½ c.c. for the second injection. But it goes without saying that the immunity conferred by reduced vaccination will be correspondingly *weaker and less lasting.*

Some medical officers, guided by the vigour of the subject, have given two injections of vaccine T, the first consisting of 1½ c.c. or 2 c.c., and the second of 2 c.c. or 3 c.c., without observing any abnormal reactions (Major J. Louis).[1]

2. *Antiparatyphoid A and B*, containing 500 millions of each of the bacilli per c.c.

1st injection 1½ c.c.
2nd „ 2 „

3. Triple *mixed* vaccine, antityphoid and antiparatyphoid A and B (*T.A.B. vaccine*), containing 500 million typhoid bacilli and 250 millions of each of the paratyphoid A and B bacilli.

Complete vaccination { 1st injection 1½ c.c.; 2nd „ 2 „; 3rd „ 2 „; 4th „ 2 „

[1] Some soldiers belonging to a company at the Front received by mistake *20 c.c.* of the same vaccine at one time—*i. e. 10–15 thousand million bacilli*—without any complications beyond numerous marked febrile reactions. Of course this is not an encouragement to imitate this practice. An instance of a similar error had been previously published. A young lady who had been given 20 c.c. and two children who had been given 10 c.c. had a moderate febrile reaction (101·2° F.), but severe pain locally (H. Vincent).

If *reduced* vaccination is performed, the first three injections should be given.

Vaccination has been performed with large doses or with ether vaccine of high potency on a large number of soldiers, in *two* injections or even in a *single* injection. The reactions have not been more numerous and the preventive results have been excellent.

As has been said, the No. 2 ether vaccine contains 2000 million bacilli, or 1000 million typhoid bacilli and 500 million each of paratyphoid A and B bacilli. The doses to be injected are—

1st injection 1½ c.c.
2nd „ 2 „

The dose used for vaccination with a single injection is 2½ c.c.

Antityphoid vaccination and antiparatyphoid vaccination, whether separately or combined, may be performed during pregnancy in healthy women, and in children. Children aged two years and even eighteen months have been inoculated.

Children tolerate injections of vaccine remarkably well.

The doses of antityphoid vaccine or of the mixed vaccine to be given are as follows—

Child of	2–4	years	one-quarter	of the	adult dose.
From	5–7	„	one-third	„ „	„
From	8–12	„	one-half	„ „	„
From	13–16	„	two-thirds	„ „	„

In giving these doses the state of development of the children should be taken into account.[1]

As carried out under normal conditions and aseptically in young and healthy subjects *who are not suffering from fatigue or incubating a disease, mild or severe,* and in conformity with the ordinary rules (complete

[1] Children 11–12 years of age were vaccinated with the T.A.B. vaccine by Dr. Pilod during an epidemic in the army zone in the north of France, and received the same doses as the adult without ill effects. In children of this age, therefore, the prescribed doses may be increased and only two injections given.

rest for forty-eight hours, a light meal, abstinence from spirits or alcoholic drinks), injections of vaccine are followed by a relatively small number of febrile reactions, which is on the average 2 per cent. The pains in the limbs and headache are very soon relieved by one or two cachets of aspirin, each containing 0·50 cgm. Only one out of 400 or 500 persons has a temperature of 104° F., and even that is not always the case. Lastly, it may happen about once in 30,000 injections that through some of the vaccine penetrating a vessel there is immediate absorption of the vaccine, and shivering, fever, headache and vomiting at once develop. Rest in bed, Rivière's potion, and when the vomiting has ceased, small doses of aspirin (0·15–0·30 cgm.) every quarter of an hour cause the temperature to drop and bring the symptoms to an end. Some vaccinal reactions accompanied by hypotension, may be successfully treated by injection of ½ milligramme of adrenalin.

Experience gained from its use in millions of individuals proves that antityphoid vaccination is inoffensive (Bousquet, Ameuille and Brulé, Maurange, Chalchat, etc.).

Complications have been observed after every kind of vaccine in the armies of different countries. They really concern men who were suffering at the time of, or shortly after, vaccination from acute or chronic infectious diseases of grave prognosis (cerebro-spinal meningitis, pneumonia, broncho-pneumonia, suppurative pericarditis, suppurative peritonitis following appendicitis, chronic myocarditis, chronic aortitis, nephritis, and pleurisy), which have nothing to do with vaccination or vaccine.

It is therefore necessary to examine the individual carefully before vaccination.

It should be realised that identical observations have been made in *unvaccinated* soldiers, whose names were down on the vaccination lists and were on the point of being vaccinated. It not infrequently happened that these men suddenly fell ill and died some days *before*,

or even *on the day before*, or *some hours before* the time fixed for their vaccination. The lesions found post mortem were also those of meningitis, pulmonary or renal congestion, pneumonia, broncho-pneumonia, suppurative peritonitis, acute or chronic nephritis, etc. In twelve out of one hundred cases the lesions were insignificant, in spite of the severity and rapidity of the symptoms seen during life in these unvaccinated subjects. Fulminating or hyperacute forms of cerebro-spinal meningitis or poliomyelitis are often responsible for these sudden deaths, and the diagnosis is all the more difficult as macroscopic lesions have not always had time to form.

These facts show that, in presence of abnormal symptoms observed in a vaccinated subject, their cause should always be sought for in a concomitant morbid or infectious state independent of vaccination. Too much care cannot be taken to avoid attributing to vaccination diseases which may occur during the eight, fifteen or twenty-one days required for immunisation.

The successful results of preventive antityphoid vaccination are well known. In the French army and navy, as well as in the English, Italian and Japanese armies, all the published reports agree in showing the remarkable protection conferred by vaccines. It has been the same during the present war.

Antityphoid vaccination was employed in the English army in India after the memorable experiments of A. E. Wright. The German army made use of it much later, in 1904–1907, at the time of its expedition against the Herreros. During the Russo-Japanese war a certain number of vaccinations were carried out in the Russian sanitary formations.

In the United States antityphoid vaccination has been compulsory in the army and navy since August 28, 1911.

In the English army, before the war, antityphoid vaccination, though voluntary, was used in 90 per cent. of the soldiers in India. A few cases of paratyphoid fever appeared there, but typhoid fever has considerably decreased.

SOME EXAMPLES OF ANTITYPHOID VACCINATION

	Incidence per 1000		Mortality per 1000	
	Non-vaccinated	Vaccinated	Non-vaccinated	Vaccinated
English Army in India (1906–1908)	23·33	3	3·93	0·36
English Army in India (1910)	13·9	4·7	2·6	0·6
English Army (India, Egypt, Malta, Crete, etc.)	30·4	5·39	16·9	8·9
English Army in India (1911)	5·3	1·7	0·4	0·09
English Army (1914–Jan. 1915)	11·11	1 injection: 83 cases. 2 injections: 33 cases.		
German Army (War with the Herreros)	99	51	12·8	6·47
American Army (1910)	6·05	0·48	0·46	0
Japanese Army	14·52	1	1·66	0·28
French Army (Eastern Morocco)	64·97	0	8·35	0
French Métropole Army (1912)	2·22	0	0·30	0
French Army, Algiers and Tunis (1912)	12·14	0·09	1·88	0
French Army, Eastern Morocco (1912)	38·23	0	5·51	0
French Army, Western Morocco (1912)	168·44	0·18	21·13	0 09
French Army, Colonial Army Corps	6·34	0	0·58	0
French Army, Avignon epidemic (1911)	225·61	0	32·02	0
Paimpol epidemic (civilian population), (1912)	41·66	0	4·58	0
Puy l'Evêque epidemic (civilian population), (1912)	52·85	0	7·14	0
Italian Army (1912)	35·3	0·3	7·1	0
Italian Army (1913), Cyrenaica		0·29		0
Italian Army (1913), Tripoli		0		0

We have already stated that triple vaccination with the antityphoid and antiparatyphoid A and B vaccine

has been used in the French army since 1910. This triple vaccination with the Val de Grâce vaccine protected the soldiers who were inoculated in Eastern Morocco in 1911 against the three diseases.

Vaccination with T.A.B. vaccine was carried out in West Morocco, where the severity of typhoid and paratyphoid infections is well known. It was found that the mixed vaccine had a very powerful immunising action on the three diseases, whereas in the civil population of Morocco the non-vaccinated continue to provide numerous severe cases. French troops sent to Morocco at the beginning of the war with Germany, who could not be vaccinated owing to the necessities of the war, only managed to escape a severe epidemic—which began a fortnight after their arrival—by means of rapid vaccination.

In like manner, German prisoners sent to Morocco would have paid a heavy toll to typhoid fever if vaccination had not cut short the commencement of the epidemic. Their sanitary condition since then has remained excellent.

In Algeria, inoculation with the triple vaccine (T.A.B.) has conferred a remarkable immunity on the troops stationed in this country, where typhoid is so rife (E. Sergent and L. Nègre).

The Italian army also employed in 1912 and 1913 vaccination by the triple ether vaccine, or T.A.B., in Tripoli, Cyrenaica, and in Italy. Publications on the subject have been made by the medical Inspector-General Ferrero di Cavallerleone, and an official report has been communicated by Professor Santoliquido, Director-General of Public Health in Italy.

The vaccinations have been performed in Italy with the mixed T.A.B. vaccine, with three injections. The vaccinations were carried out in two periods: September 1912–June 1913, and June 1913–December 1913. In the first period the vaccines of Pfeiffer-Kolle and Vincent were used, in the second Vincent's T.A.B. vaccine almost exclusively, which had been prepared at the Milan Institute of Serum Therapy.

In the Libyan expeditionary force the non-vaccinated showed a morbidity of 35·3 per 1000 and a mortality of 7·1 per 1000.

In the first period 4682 injections were given with the Pfeiffer-Kolle vaccine, and 11,509 with the triple ether vaccine. In the second period 11,703 injections were given.

A platinum loopful of a culture on agar being taken as unity, as German bacteriologists advise, the doses inoculated were as follows—

	1st injection	2nd injection	3rd injection
Vincent's vaccine	0·40	0·90	1·20
Heated Pfeiffer-Kolle vaccine .	0·50	1	2

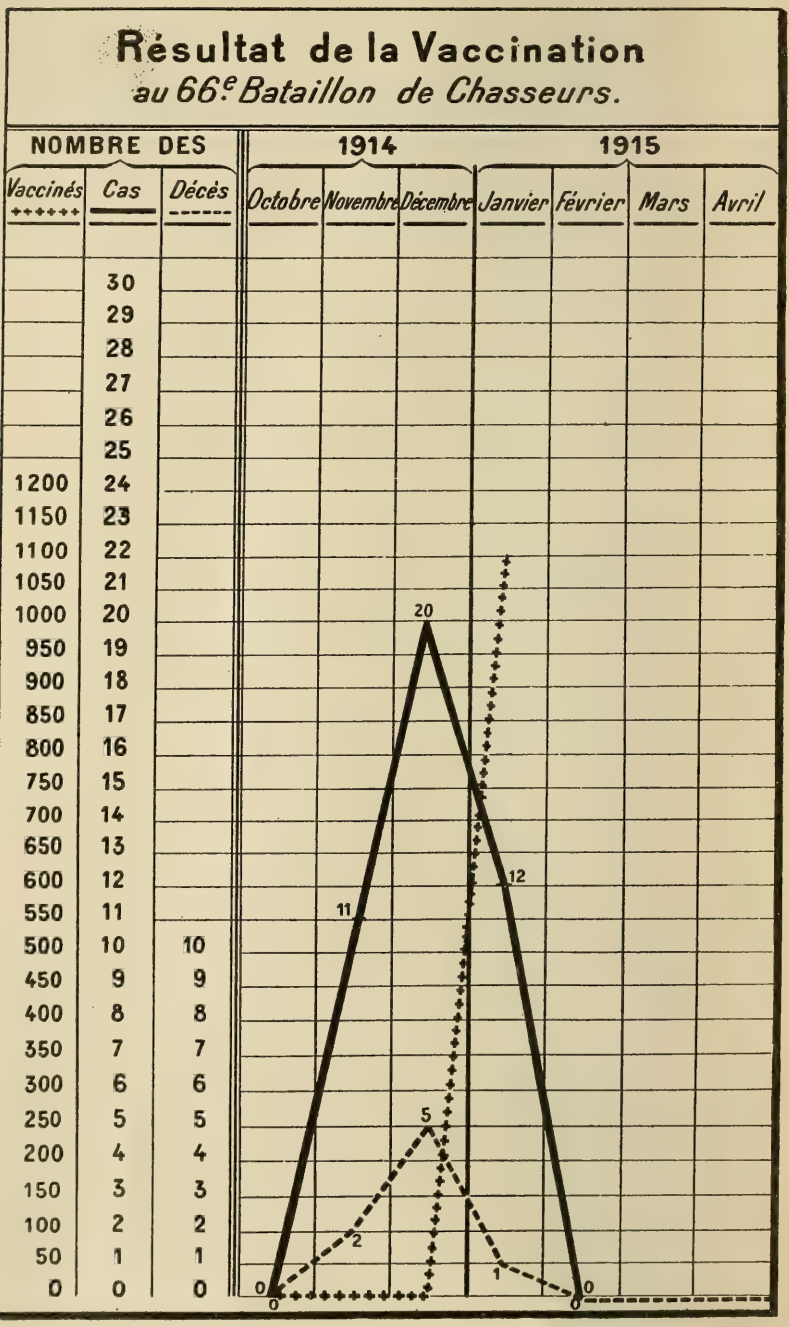
The Pfeiffer-Kolle vaccine has thus been given in much larger doses.

The statistics of the morbidity among the vaccinated in the region of North Africa, which is so severely infected by typhoid fever, have shown the same remarkable results as those in the French army, in the interior, in Algiers and Morocco, in striking contrast with the morbidity of the non-vaccinated.

Vaccinated	Number of Cases of Typhoid Fever		
	1 injection only	2 injections	3 injections
1. With the triple ether vaccine (T.A.B.)	4·4 per 1000	2·7 per 1000	0·3 per 1000
2. With the heated vaccine (Pfeiffer-Kolle)	10·7 per 1000	6·9 per 1000	7·2 per 1000

In the second period of vaccination in the Italian army, 3494 soldiers were given the T.A.B. ether vaccine. Their morbidity and mortality were as follows—

	Cases	Deaths
In Cyrenaica	0·29 per 1000	0
In Tripoli	0	0


Résultat de la Vaccination
au 66e Bataillon de Chasseurs.
NOMBRE DES
Vaccinés
Cas
Décès
1914
1915
Octobre
Novembre
Décembre
Janvier
Février
Mars
Avril
30
29
28
27
26
25
1200
1150
1100
1050
1000
950
900
850
800
750
700
650
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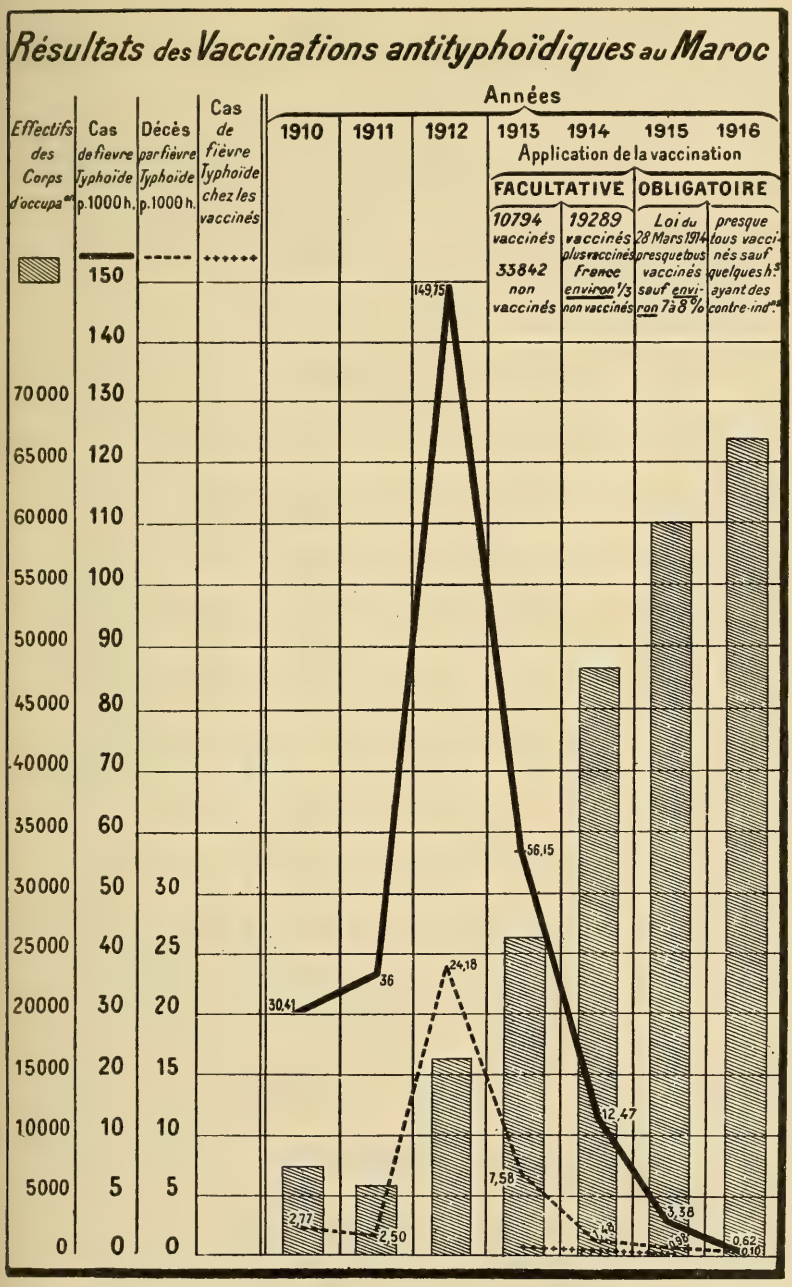

Résultats des Vaccinations antityphoïdiques au Maroc
Années
1910
1911
1912
1913
1914
1915
1916
Application de la vaccination
FACULTATIVE
OBLIGATOIRE
10794 vaccinés
33842 non vaccinés
19289 vaccinés plus vaccinés France environ 1/3 non vaccinés
Loi du 28 Mars 1914 presque tous vaccinés sauf environ 7 à 8 %
presque tous vaccinés sauf quelques h.s ayant des contre-ind.s
Effectifs des Corps d'occupation
Cas de fièvre Typhoïde p. 1000 h.
Décès par fièvre Typhoïde p. 1000 h.
Cas de fièvre Typhoïde chez les vaccinés
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
5
0
30
25
20
15
10
5
0
30,41
36
149,75
56,15
12,47
3,38
0,62
0,10
24,18
7,58
1,48
0,90
2,77
2,50

As the result of these observations, Ferrero proposed that vaccination should be made compulsory in the Italian army.

Antityphoid vaccination has been made compulsory in the French army since March 28, 1911, on the proposal of Léon Labbé. The navy adopted the same measure in November 1914. Shortly afterwards the Belgian War Minister took a similar decision.

Since the war began simple or mixed vaccination has been adopted by all the belligerents.

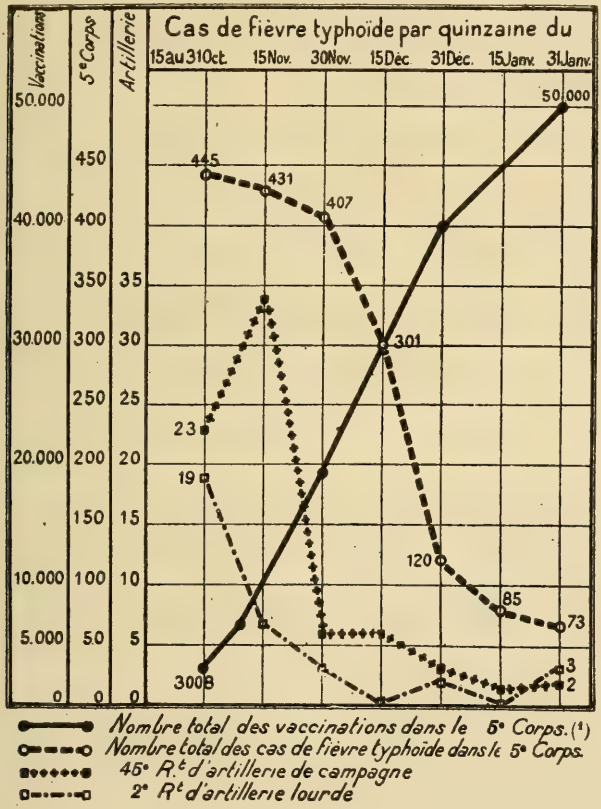
It may be asserted that in spite of the occasionally very unsatisfactory conditions under which it has been practised in France, in spite also of the difficulties of controlling the vaccinations and the actual nature of the infections (typhoid fever, paratyphoid fever, enterococcus infection, and various other infections), preventive vaccination has succeeded in saving the French army a very considerable number of cases and deaths. Reduced vaccination, although involving a correspondingly reduced immunity, has nevertheless conferred considerable protection on the corps among which it could be applied from the first, *e. g.* 5th Corps (Javal), territory of Belfort (100,000 vaccinated: Bousquet), 4th army, 5th army, 77th, 98th, 235th, 243rd, 364th divisions, etc., as well as infantry regiments in the Belgian army.

The circumstances of the present war did not at first permit of the universal employment of preventive vaccination in the army. But as soon as this method was introduced and submitted to control, the epidemic curve in the armies was found to drop suddenly and to remain subsequently at a very low level. Ever since 1915 mortality due to typhoid diseases has been very low, and the sanitary condition of the army has for a long time been superior to that in peace time. The Russian brigades which have been vaccinated in France with from 1 to 3 injections have also enjoyed a remarkable immunity.

Owing to the nature of the military operations, the continual stagnation of the troops in the trenches and

cantonments, the enormous effectives engaged, and the long duration of the war, it may be calculated that specific vaccination has saved the country "an extraordinary proportion of cases" and an extremely high number of deaths.

Before the war with Germany (we have no need to



allude to the now classical example of the Avignon epidemic in 1911, when among 687 non-vaccinated soldiers there were 155 cases of typhoid fever with 22 deaths, whereas among 1366 completely vaccinated there was not a single case of this disease), a young doctor who had been vaccinated during the incubation stage had a suspicious febrile gastric attack. Three

mild cases also appeared after the first or second injection in men who were in the incubation stage, and consequently already infected at the time that the injection was made.

EPIDEMIC OF AVIGNON (1912)

Present numbers of the garrison	2053
Number of vaccinated soldiers—	
1. Before the epidemic	525
2. During the epidemic	841
Total number vaccinated (ether vaccine)	1366

DEATHS FROM TYPHOID FEVER

	Cases		Deaths	
	Number	Incidence per 1000	Number	Incidence per 1000
Non-vaccinated 687	155	225·61	22	32·02
Vaccinated 1366	0	0	0	0

The following year the complete garrison of Avignon, containing 2420 men, was vaccinated, and there was no case of typhoid fever. Among the soldiers in this town, from 1892 to 1912 inclusive, there had been 1263 cases of typhoid fever and 118 deaths. In 1913 all these figures were reduced to zero.

Similarly conclusive observations were made on the occasion of the military epidemics of Larissa (Greek army, 1912), Marseilles, Issoudun, Tours, etc.

At Tours a severe epidemic of typhoid fever occurred in January–February, 1914. A single company of the 66th infantry regiment had 37 cases out of 180 men. The company was vaccinated at once and the epidemic ceased, but it appeared again in the other companies. Influenza, scarlatina, mumps, and cerebro-spinal meningitis were prevalent at the same time. Nevertheless, the whole regiment was vaccinated, and the epidemic was thereby brought to an end. This epidemic

was almost comparable in severity to that of Avignon. The figures are as follows—

Tours Epidemic		Cases		Deaths	
		Number	Proportion per 1000	Number	Proportion per 1000
Non-vaccinated	488	96	199	21	43·40
Vaccinated	1646	0	0	0	0

The vaccinations carried out in the civil population at Avignon (400 inhabitants), Puy l'Evêque (Lot), Paimpol, etc., on the occasion of severe epidemics gave rise to the same conclusive observations. In a certain number of places or towns, *e. g.* Grans (Bouches-du-Rhône), Rouffignac (Dordogne), Alais, Egletons (Corrèze), Sermaizes (Loiret), Ymouville (Eure-et-Loir), Andilly and Margency (Seine-et-Oise), Donges (Loire-Inférieure), etc., the protection acquired by the vaccinated proved to be remarkably complete.

We may quote as an example the cases of the epidemic observed at Largeau (Loiret), from June to September 1913, by Dr. Grancher. This epidemic was due to milk, and fourteen families making use of the infected milk were attacked. Dr. Grancher vaccinated the members of seven families with Vincent's vaccine, and the other seven refused. The result was that typhoid fever continued for three months by means of contagion from person to person in these families, among whom it caused fearful ravages, all—or almost all—their members being attacked in succession. In one of these families seven persons out of eight had typhoid fever in succession. The grandmother alone, aged seventy-two, escaped. On the other hand, the inhabitants (eighty persons, including forty women and eight children) who had been vaccinated even partially were entirely protected against infection.

At Sivas (Turkey in Asia), Seville (Prof. Juan Peset), where 624 persons were vaccinated, Noguer (Spain),

the Belgian Congo (Dr. de Ruddère, Dr. Polidore and Dr. Valche), Medellin (Columbia), Connixheim (Belgium), etc., similar examples of immunity have been observed.

A very important fact is that when the inoculations are rapidly carried out on all the persons liable to infection, they exercise an arresting action upon the epidemic, which dies down rapidly when the second or third injection of vaccine has been given.

The statistics published by Leishman for the English army in India and the other colonies, by Russell for the United States army, etc., testify, with the authorities already quoted, that *specific vaccination is the most powerful prophylactic measure which we possess against typhoid fever.* From this point of view it may be compared with vaccination against smallpox.

Before concluding, it seems imperative to insist on the absolute necessity of applying vaccination rigorously to obtain all the effects which one is entitled to expect from it. The difficulties in practice due to the state of war are obviously great.

Furthermore, the frequency with which the soldiers to be vaccinated are leaving or changing their billets explains the fact that vaccination in war time may be carried out incompletely, or improperly registered or controlled. Errors are likely to be all the more numerous as enormous bodies of men are being dealt with. We cannot, therefore, too frequently repeat the advice to conform minutely to the practical rules for vaccination, to enter each of the injections carefully and with rigorous exactitude on the vaccination card, and to keep a record of it in a special register.

During the arrival in large numbers of men to be vaccinated, either in barracks or at the Front, numerous causes of error may arise, such as entering men absent or postponed on the list of those actually vaccinated, hasty signing of certificates, frauds due to the soldiers, any one of whom for a consideration will take the place of another and reply when his name is called out, while

others imitate the Medical Officer's signature and reproduce it in their books, or obtain an inaccurate certificate from an obliging orderly. The attention of Medical Officers who perform the vaccination should be called to these facts, and to their frequent results. Inquiry, in fact, has proved the great frequency of mock vaccinations in war time.

It will be well to remember that many soldiers confuse vaccination against smallpox with antityphoid vaccination—Wright formerly drew attention to the same occurrence in the English army—and a large number still appeal to a vaccination which does not exist to escape injections.

Medical Officers who are entrusted with the carrying out of vaccination should provide themselves with reliable assistants, and take the greatest care not only in the technique of the injections and previous examinations of the subjects to be vaccinated, but also in everything concerning the verification of the states of vaccination, the exact control of the injections performed, with their dates and doses, the registration of the absent, sick, and those on leave; for any neglect or forgetfulness may result in attributing an undeserved failure to this successful method, and, what is more serious, in exposing soldiers to a dangerous infectious disease, the prognosis of which is often fatal.

SECTION II

DYSENTERY ASIATIC CHOLERA AND EXANTHEMATIC TYPHUS

DYSENTERIES

PART I.—CLINICAL SURVEY

CHAPTER I

SYMPTOMATOLOGY

THE term *dysentery* serves to denote a symptom complex which indicates an ulcerative colitis, acute or chronic, which may be due to various pathogenic agents, such as dysentery bacilli, amœbæ, etc.

These affections, etiologically quite distinct, are contagious. They present some common symptoms, and each of them possesses its special symptoms.

The dysenteric syndrome comprises three essential symptoms common to all dysenteries :

1. Abdominal pains.
2. Tenesmus.
3. Stools presenting a characteristic appearance.

1. **Abdominal Pains.**—The abdominal pains are spontaneous or provoked. The spontaneous pains manifest themselves as *colics*, sometimes generalised throughout the abdomen, sometimes localised in the umbilical region or the left iliac fossa, and by extremely severe griping pains (tormina), which follow the entire course of the colon as far as the rectum. In slight cases the griping pains are transient, occurring at the moment of alvine evacuation, diminishing immediately after evacuation and then disappearing. In more serious cases they are much more frequent, and may occur in the absence of any evacuation. Pressure exerted on the large intestine causes a more or less acute pain, especially in the region of the left iliac fossa. It is often possible, by the localisation of the pains thus produced, to map

out the extent of the intestinal surface affected. Abdominal pains may be absent in cases which are from the first very serious (Dutroulau). They become progressively less severe, having at first been rather violent, to disappear completely when gangrenous lesions occur.

2. Tenesmus.—The patient is aware, in the slighter cases, of a feeling of weight, of a foreign body in the rectum; but most frequently there is a painful feeling of tension and constriction in the region of the anus, with an incessant call to pass stools. Sometimes a number of false calls are followed by fruitless efforts (tenesmus); sometimes the straining results in the expulsion of a very small quantity of excrement (barely a teaspoonful). Each attempt causes extremely violent pains (smarting, burning, tearing sensations), recurrences of these being provoked by the slightest incidents, such as coughing, sneezing, deglutition, etc.

The sum of these sensitive disorders, localised in the terminal portion of the rectum, constitutes *rectal tenesmus*, which, in a number of cases, is accompanied by analogous symptoms affecting the bladder (*vesical tenesmus*).

Rectal tenesmus is frequently complicated by paralysis of the sphincter and the levator ani (Trousseau, Colin); repeated efforts to defæcate may cause prolapse of the rectum, an accident common in children.

The intensity of the tenesmus varies greatly in different patients. In hot countries tenesmus is said to be often absent, or transient, and is confined to a mere sensation of smarting; it is said to be infrequent in India. According to Sir Patrick Manson, the nearer the lesion to the rectum, the more severe the tenesmus; the nearer to the cæcum, the more violent the colic. These two symptoms, in addition to the presence of painful spots, constitute, in the majority of cases, a reliable guide to the localisation of the lesions and to an estimate of their extent.

3. Dysenteric Stools. — Constipation being the general rule in confirmed dysentery, the true dysenteric stools contain little or no fæcal matter. Their varying aspect has given rise to numerous comparisons. Sometimes they consist of transparent and whitish mucus, diffluent, of a membranous aspect, twisted, or wound into viscous masses, and have been compared *to scrapings of the bowels* (Jaccoud); sometimes the mucus is flaky, or in rice-like grains, or in punctiform debris, or the matter excreted has the appearance of *frogs' spawn* or the white of raw eggs. The stools are usually blood-stained, owing to the extension of the ulcerative process to the vessels of the intestinal wall. In these cases the blood merely streaks the mucus, or appears on its surface in the form of patches of varying extent, or again, it is so intimately mixed with the mucus that the stool resembles the *rusty sputum* of the pneumonic patient.

Sometimes the mucus, scanty and sanguinolent, floats in a serous liquid, of a pink or reddish colour; it has been described as resembling water in which raw meat has been washed. In other cases the hæmorrhagic stools consist of almost pure blood, red and fluid or black and mingled with clots. Lastly, they may be *gangrenous*. Shapeless shreds of sphacelated mucus float in a serous liquid, reddish, brown, or black, with a horrible smell.

Kelsch has very justly remarked that the alvine dejecta reflect, by their aspect and their nature, the degree and the nature of the intestinal lesions.

The number of stools is always considerable in dysentery: 10, 30, 50, and even more in the twenty-four hours; 160 to 180 in a case of Trousseau's; 200 in twelve hours in a case of Zimmerman's.

The stools are more frequent at night than in the day. The matter expelled each time is by no means abundant, especially at the outset; it becomes more copious as the malady develops. Barely a hundred grammes (about $3\frac{1}{2}$ oz.) in benign cases, it may amount to several litres in cases of bilious dysentery.

The mucus has a stale or putrid odour, and its reaction is alkaline.

Such is the dysenteric *syndrome* common to all dysenteries, whatever their infectious agent. Many of these exist, and they can be determined only by investigation in the laboratory.

We may distinguish, in the first place, among the acute forms of dysentery, two forms which are clearly defined, and which are by far the most frequent :

1. Bacillary dysentery.
2. Amœbic dysentery.

In the second place, we find dysenteric conditions due to various other etiological agents : spirilla, coccobacilli, *Bacillus pyocyaneus*, *Balantidium coli*, *Schistosoma mansoni*, *Chilodon dentatus*, etc., which have all to be investigated.

We shall here consider bacillary and amœbic dysentery.

I. Bacillary Dysentery

The clinical development of bacillary dysentery comprises a period of incubation, a period of onset, an acute dysenteric period, and a terminal period.

1. Period of Incubation.—This period is generally of brief duration : forty-eight hours (Strong and Musgrave), or two to three days (Lentz). In experimental infections of man effected by Strong and Musgrave and others, the first symptoms manifested themselves twenty-four hours after the ingestion of the culture of dysentery bacilli.

2. Period of Onset.—Very rarely a prodromal period is observed, characterised by mucous or bilious diarrhœa. In reality it constitutes the first stage of the infection. This premonitory diarrhœa, when it exists, lasts barely twenty-four to thirty-six hours.

As a general rule, dysentery makes its appearance suddenly, without prodromes, and in a few hours the acute period is established.

3. Acute Dysenteric Period.—In the slightest cases the affection amounts to a diarrhœa of ordinary appearance. The stools are not numerous and contain only traces of mucus. In this category are contained a certain number of cases of summer diarrhœa, with abdominal and rectal pains which are scarcely noticeable, a fair number of cases of infantile diarrhœa, and also certain cases of "trench diarrhœa."

Most usually the patient experiences, at the outset, vague abdominal pains, followed by more violent colics, with a sensation of fulness in the region of the rectum, which brings on a more and more imperative call to stool. Then the dysenteric syndrome sets in in all its intensity: colics, straining, tenesmus and characteristic stools. At this stage the patient may suffer from nausea, hiccough and mucous or bilious vomiting. The abdomen is retracted and painful; the urine, which is diminished, often contains albumin; the tongue is dry; the liver congested, and increased in volume, and painful under pressure, especially in the region of the gall-bladder.

Fever may be regarded as exceptional during dysentery. When it is present it rarely exceeds 102·2° F., and shows itself only during the first three or four days of the disease.

The malady may develop with a grave prognosis, and may even terminate in death, without a considerable rise of temperature; hypothermia may be observed in the very toxic forms.

The pulse is generally frequent, small, and often irregular. The face is pale and dejected; emaciation is often rapid and very pronounced.

4. Terminal Period.—In favourable cases, after an average of three to ten days, the colic and tenesmus become less severe. The stools, less frequent, lose their dysenteric character and become fæcal. Occasionally there is an intestinal flushing, of a bilious or serobilious nature, which continues for some days. Then

the stools gradually resume their normal appearance and consistency. At this stage constipation may be met with, and after this a relapse may occur.

Sometimes, at the beginning of the convalescent period, increased sweating and an increase in the amount of urine is observed; these may even assume the characters of a true crisis.

The patient's strength recuperates slowly; sometimes the convalescence is longer than the malady.

Bacillary dysentery is benign, of medium severity, or severe. In certain cases the dysentery is serious from the outset; in others grave complications may appear during the course of a benign dysentery, which modify its development. It ends in recovery or death.

Clinical Forms of Bacillary Dysentery

1. The Light Form.—Dysentery may often present the appearance of an ordinary diarrhœa. The patient suffers from a certain amount of nausea, the tongue is clammy and resembles that seen in indigestion, and the abdominal pains are not very pronounced; the stools are not very frequent—4 to 6 per diem—and contain only traces of mucus, which may easily pass unperceived. The affection lasts a few days only, and its dysenteric nature is most frequently unrecognised.

2. Bilious Form.—The malady commences with a violent gastric disturbance, with congestion of the liver, vomiting, and very abundant bilious diarrhœa. After the lapse of a few days the stools, turgid and frothy, contain slimy mucus coloured with bile. Jaundice is generally observed.

3. Fulminating Form.—The onset is sudden, in the middle of the night, with more or less violent rigors, vomiting, severe headache, and a rise of temperature to 102° or 104°. At the same time the stools assume the dysenteric character. In the space of two or three days to a week (approximately), the fever persisting to the

end, collapse sets in with hypothermia, and the patient expires. In certain cases death may occur even before dysenteric stools are passed, so virulent is the intoxication (Manson).

4. Ulcerative Form. — The stools, after a benign commencement, become fetid, and contain not only blood, but also a more or less voluminous gangrenous debris, of a greyish hue, with a putrid odour.

This denotes the existence of deep ulcerations, which are slow to cicatrise, and tend to set up a relapsing dysentery.

5. Gangrenous Form.—This is observed in tropical regions; very rarely in temperate countries. From the outset it is a very serious malady. The stools are incessant; the pains, which are excruciating, spread in all directions, not only through the abdomen, but also along the course of the sciatic nerve and in the region of the testicles (Le Dantec). Tenesmus is very severe; the temperature may be febrile, the face pale, shrunken and altered, the eyes sunken. The general condition is bad, the voice feeble, the pulse small and thread-like and slower than the normal. There is incessant vomiting and a pathognomic hiccough sets in.

The stools, at first blood-stained, shortly assume the gangrenous type described above. At the same time the pains abate, even disappearing completely, and the patient feels better. This improvement is deceptive, for the vital powers are failing; the heart grows weaker and the pulse becomes barely perceptible. The skin grows cold and cyanosed, and is covered with a clammy perspiration. The mind remains clear, though a little less active, and the patient slowly expires without a death struggle, without suffering, unless he is suddenly carried off by a syncopal attack. Death is the usual termination of gangrenous dysentery. However, in rare instances, recoveries have been reported (Dutroulau, Laveran, Berenger-Feraud, etc.).

6. Choleraic Form. — In Cochin-China a form of dysentery is occasionally observed with vomiting, cyanosis, collapse, algidity, muscular cramps, suppression of urine, and a "broken" voice, these giving the patient an aspect comparable to that of cholera. During the present war P. Remlinger and J. Dumas have observed in 4 per cent. of cases—in benign cases as well as in those which were serious from the first—at the outset, or when the malady is established, or during convalescence, an acute supra-renal syndrome recalling cholera. In a few hours the patient literally "melts away." He appears fleshless, skeleton-like, the eyes sunken, the nose sharp, the abdomen hollowed like a boat. There is cyanosis, the temperature falls; the pulse, frequent and compressible, is imperceptible or nearly so. The heart sounds are remote and muffled, often of an embryocardiac type. The tongue is dry; the patient has an inextinguishable thirst, with hiccough, nausea, vomiting; his voice is broken; he has cramps; and there is abundant and very liquid diarrhœa. The evacuations are sometimes involuntary. There is oliguria, or even anuria. The patient becomes prostrated and plunged into a condition of semi-somnolence. Death follows rapidly. The above-named authors have found histological lesions in the supra-renal capsules, which are two to three times larger than usual.

7. Typhoidal Form.—This form is characterised by high temperature, dryness of the tongue, abdominal meteorism, stupor, delirium, ataxo-adynamic phenomena, and in children by convulsions. The stools, dysenteric during the first week, afterwards become diarrhœal. Although these forms occur most frequently apart from any association with typhus or typhoid fever, it must not be forgotten that in the course of all wars, and notably during the present war, cases of mixed infections have been recorded, such as those of typhoid fever and dysentery (Remlinger).

8. Hæmorrhagic Form.—This form of dysentery, which is hæmorrhagic from the commencement, is rare. Le Dantec has observed one case, which was quickly fatal. Most frequently the hæmorrhage is intestinal; it has the same pathogeny as the hæmorrhage of typhoid fever. It may occur at any stage of the disease, and is usually accompanied by typhoid-like symptoms. A sudden collapse may result, even in cases otherwise benign. Kelsch and Kiener include under this form all cases with marked or serious hæmorrhage, whether of the intestines, the mucous membranes, the cellular tissue, or the skin.

9. Long-continuing or Relapsing Form.—Recovery after severe or serious cases of dysentery may be apparent only. Often the stools become irregular, while digestion is difficult and painful, accompanied by colic and slight diarrhœa of variable aspect (mucous, bilious, serous, sanguinolent, sometimes fetid). The abdomen remains sensitive, the patient slowly becomes cachectic, and dies at the end of a few weeks, or else, after a departure from strict diet, or after a chill, or fatigue, an actual relapse occurs, which develops as in the original attack. Thus there may be alternate periods of quiescence and recrudescence, which may continue for a varying space of time. Recovery may be established after several months, but death is only too often the outcome either of a serious relapse or of a progressive cachexia.

10. Chronic Form.—Bacillary dysentery may sometimes, though much less frequently than amœbic dysentery, give rise to a chronic condition (H. Vincent). The patient, after an acute period of varying duration, continues, for several months, a year, or longer, to pass fluid and lienteric stools.

Their number is 3, 4 or 5 per diem, with more marked inflammatory attacks, straining, and tenesmus provoked by errors of diet, chills or fatigue. This form of dysentery is often unrecognised, above all when the

initial period of mucous and sanguinolent stools has been very short or has passed unperceived. The patient grows steadily thinner, his muscles become wasted, and he falls into a condition of marasmus, often confounded with intestinal tuberculosis.

Complications

In the course of bacillary dysentery *intestinal hæmorrhage* may be met with; this may be primary or secondary, as in typhoid fever. *Peritonitis* is not exceptional, with or without intestinal *perforation.* The most usual position of the latter is said to be the *rectum*, and after that the sigmoid flexure.

Nervous disorders (peripheral neuritis, paraplegia, monoplegia, general paralysis more rarely) are fairly frequent (Zimmermann, Trousseau, Bouillaud, Ridoux, Moutard-Martin, Gubler, Delioux, Pugibet).

Arthropathies: these may occur at any stage of acute dysentery. Sometimes they amount merely to polyarticular manifestations of brief duration; sometimes to mono- or bi-articular localisations of a more persistent character. Dysenteric arthritis sometimes assumes the character of infectious pseudo-rheumatism (Brault, Boudet); it is most frequently characterised by a painful swelling of the joints with or without effusion.

Combay has recorded a case of thrombosis of the left iliac artery with gangrene of the corresponding limb. *Cicatricial strictures* of the intestine, especially in the region of the rectum, are comparatively frequent complications. Invagination, intestinal occlusion, and internal strangulation have also been reported. Remlinger has noted certain rare complications: epididymitis, and general dropsy without albuminuria. *Acute nephritis* is fairly common.

II. Amœbic Dysentery

Amœbic dysentery presents the same essential symptoms as bacillary dysentery. Long regarded as peculiar to tropical or semi-tropical regions, it has been observed in all parts of Europe, and during the present war numerous cases have been observed in France (Ravaut and Krolunitsky, Job, Richet junior, Rist, Rathéry, Rives and Huet, Lian and Lyon-Caen, Orticoni and Ameuille, Job and Hirtzmann, etc.). It is characterised by its tendency to relapse or assume the chronic form, by its irregular development, consisting of periods of quiescence and exacerbation, and, lastly, by the frequency of hepatic complications (simple congestion or abscess of the liver).

It may commence suddenly, develop in an acute form, and end in death or recovery in a comparatively short time. This is the less usual form.

The commencement is almost always insidious, often marked only by a *simple diarrhœa*, painless and hardly inconvenient. The dysenteric syndrome makes its appearance in the course of a few days and the patient appears to improve. But as a rule this improvement is only apparent. After a period of varying duration a series of relapses occurs, and the malady becomes *chronic*.

Abdominal pains along the course of the large intestine are constant. They may be elicited by pressure, especially in the region of the ulcerations—namely, the cæcum, the hepatic flexure, and the sigmoid flexure. When they are localised in the latter portion of the large intestine the ulcerations are particularly painful, provoking rectal and vesical tenesmus, and frequently recurring efforts which are not always followed by evacuation.

Alternatively, the patient passes diarrhœal stools, sometimes absolutely liquid, sometimes soft and doughy, and then frequent dysenteric stools, especially during the night, with tenesmus and colic. The mucus evacuated is whitish or greyish, more or less

streaked with blood on the surface. In it we find red corpuscles and leucocytes, many of which are eosinophile (Billet). This latter fact has not, however, always been confirmed. The odour of the mucous discharges is sometimes stale, sometimes fetid; their reaction is alkaline (H. Vincent). Jaundice is common. Digestion is painful and difficult, and there may be frequent vomiting. The general condition of the patient grows worse and worse, his emaciation more and more perceptible, although the appetite may be fairly well maintained. If complications are of some duration, the patient becomes cachectic. His skin is dry, wrinkled, and assumes a bronzed and earthy tint; there is no perspiration, the urine is scanty, and its emission is sometimes painful. The temperature may sink below the normal, as low as 93·2° in the axilla. The patient is like a living skeleton, and he dies of inanition, unless he is carried off by an acute crisis, an attack of intestinal gangrene, tuberculosis, or a secondary infection.

Chronic dysentery is of extremely variable duration, lasting from a few months to many years.[1] It may ultimately end in complete recovery, without sequelæ. Very frequently relapses are observed after a few days, a few months, or even a year (H. Vincent). Chronic and long-continuing forms are particularly refractory, often leaving behind them severe dyspepsia, extreme weakness, emaciation, and even lesions (destruction of glands, thickening of the intestinal walls, cicatrices, adhesions, strictures, etc.), so that the health of the patient afflicted with them is usually jeopardised.

Complications

The fact that the development of amœbic dysentery is generally prolonged explains the multiplicity and the nature of the complications which have been observed in the course of this disease.

[1] Cases have recently been reported where the infection had lasted for 20, 26, and 30 years.—Ed.

Among these complications may be mentioned *peritonitis*, localised, extensive, or general, which is often discovered at autopsy, with or without perforation; *intestinal perforation*, which is of very frequent occurrence (being found in 12 out of 77 autopsies conducted by Strong), and which is localised principally in the neighbourhood of the sigmoid flexure; *thrombosis* of the large blood-vessels; partial *paralysis*; *infarctions*, and *abscess* of the spleen, the brain, etc.

The most frequent complication, which makes the prognosis of amœbic dysentery peculiarly gloomy, is *abscess of the liver*. It is never met with in the course of bacillary dysentery. The abscess is very often localised in the right lobe, which is hypertrophied. The only constant clinical indication is the excruciating pain, which must always be looked for, and which is provoked by pressing deeply at any point in the region of the thorax, principally between the ribs. When the abscess begins to form the patient experiences and complains of discomfort and pain in the liver, very often *radiating to the right shoulder*, and a painful heaviness in the region of the right hypochondrium. The swelling may be apparent. There is emaciation and jaundice, the latter in one case out of every four. There is now reason to suspect suppurative hepatitis, especially if there is fever. Pleurisy of the base is rarely absent. Diagnosis is sometimes facilitated by radiography and, if needful, by deep exploratory punctures, but it is often difficult to localise the abscess if of small volume or in an early stage of development. It is useful to examine the blood. In the course of amœbic dysentery sometimes a very appreciable eosinophilia of the blood is noted (4 to 47 per cent.) (Billet, Chantemesse and Rodriguez, Dopter, Hoyt, C. Mathis and M. Leger). This eosinophilia is not, however, constant.[1] When it exists its disappearance

[1] It has probably nothing to do with the dysentery *per se* and more likely is due to helmenthic or other complications. Certainly many cases of amœbic dysentery never show it.—Ed.

enables one to mark the moment at which the dysentery becomes complicated by suppurative hepatitis. The amœbic abscess of the liver, in short, causes the diminution or even the absolute disappearance of eosinophile leucocytes in the circulating blood.

The development of the abscess is sometimes insidious, without increase of temperature, without any appreciable pain, and is marked only by emaciation, dyspepsia, and vague pains in the region of the liver. Abscess of the liver may supervene, although not always, in patients suffering from slight attacks of dysentery who have, until the formation of the abscess, undergone no treatment, or in patients treated only during the acute periods of the disease—that is to say, in an insufficient manner (Faure, Mauté). Finally, there are cases in which suppurative hepatitis constitutes the initial and even the only localisation of amœbic infection, the enteritis having been absent, or quite ephemeral. Rogers has noted the particular frequency of hepatic abscess in alcoholic subjects.

Abscess of the liver tends to effect a spontaneous external opening, either through the skin or the intestine, or into the peritoneum, or into the bronchi through a vomica; more rarely into the pelvis, the stomach, etc.

Death often ensues through cachexia or secondary infections.

During the present war abscess of the liver has often been observed to occur as a sequel of ill-defined intestinal affections treated as enteritis or "trench diarrhœa." The exact diagnosis of amœbic dysentery was only come to by the formation of the abscess and the therapeutic success of emetin (Rives and Huet, Rathéry and Bisch, Lian and Lyon-Caen, Rist and Roger, etc.).

III. Dysenteries caused by Various Etiological Agents

We shall confine ourselves in this section to the enumeration of some of the varieties of dysentery

attributed to various agents, and some of which, as we have already said, require to be made the subject of fresh investigations before their individuality can be confirmed.

Spirillum dysentery.—Le Dantec has described a dysentery in which microscopic examination of the mucous discharges reveals the presence of a pure culture of spirilla. This spirillum dysentery is said to be fairly common in the south-west of France, principally in the region of Bordeaux. It develops without fever or hepatic complications. It may become chronic, but always ends in recovery.

Cocco-bacillary dysentery.—Lesage (in China, Cochin-China, Algeria, and Toulon) and Métin (in Cochin-China) have described two cocco-bacilli, very nearly related, which may be isolated from the blood of dysenteric patients.

Dysentery due to Balantidium coli.—This has been observed by Strong and Musgrave in the Philippines, by Solaviev and Klimenko in Russia, and by Ernrooth in Finland.

Dysentery due to Bilharzia (*Schistosoma mansoni*).—This has been observed in the Congo by Firket. It is not uncommon to find the eggs of the parasite, not only in the stools of the patients, but also in the urine.[1]

Dysentery due to Chilodon dentatus.[2]—Observed by Guiart.

Various dysenteries.—Lewkowicz and Simonin believe that the *enterococcus* of Thiercelin plays an active part in many dysenteriform processes. The *Bacillus pyocyaneus*, the *Proteus vulgaris* (Macé, Mougniet), and other microbes have also been incriminated.

Finally, dysenteries have been reported as resulting

[1] The original case was described by Manson: a man from Antigua, West Indies. It is excessively rare to get lateral-spined bilharzia ova in the urine.—Ed

[2] *Chilodon dentatus* is a protozoon commonly found in water. There is no proof that it can live as a parasite or produce symptoms of dysentery.—Ed.

from Trichomonas (Billet, Simonin, Escomel), Cercomonas, *Lamblia intestinalis* (C. Mathis, C. Fairise, and Jacquot, etc), *Tetramitus* (*Chilomastix*) *mesnili* (Brumpt), *Pentatrichomonas ardindelteili* (Derrieu and Raynaud), etc. The symptomatology of these affections is similar to that of the other forms. Their development is in general chronic.[1]

[1] The flagellates of the intestine may produce diarrhœa, though some observers even deny this rôle to them. They certainly do not produce dysentery in the strict sense of the term.—Ed.

CHAPTER II

DIAGNOSIS OF DYSENTERY

I. Diagnosis of the Dysenteric Syndrome

It is necessary, in the first place, to diagnose the dysenteric syndrome. The character of the stools, their frequency, colics, cutting pains, straining, and tenesmus, are by themselves, when they are united, symptoms characteristic enough to render diagnosis easy. But it must not be forgotten that there are cases of *larval dysenteries*, hardly defined, of which " trench diarrhœa " is sometimes one of the forms, in the course of which the syndrome is represented by only one or two symptoms, which are not always pathognomic. The development of these cases, the complications which accompany them, and notably the occurrence of hepatic abscesses, permit of the establishment of a retrospective diagnosis.

It must be remembered that *rectal polypus* in children, *hœmorrhoids* in adults, and *neoplasms* in the aged, may provoke sanguinolent stools, tenesmus, and the expulsion of mucous discharges.

Retroflexions and *retro-uterine phlegmons* may, by their concomitant symptoms, simulate attacks of dysentery, and the same is true of affections of the bladder, especially of lithiasis.

The pernicious dysenteriform access [malarial dysentery], the existence of which is contested by certain authors, presents a great similarity to dysentery. The stools may be mixed with blood and mucus. There is straining, colic and tenesmus, and the temperature is often very high. Under treatment by quinine and opium the intestinal flux is replaced by abundant

perspiration, the end of the access is determined, and the diagnosis established. It is possible that the symptoms observed may be due to an association of dysentery and malaria. The examination of the blood and the stools yield valuable indications.

The chronic diarrhœa of hot countries (synonyms: Cochin-China diarrhœa, tropical diarrhœa, sprue, spruw, pilosis linguæ, white diarrhœa, tropical aphthæ, Ceylon sore mouth) sometimes presents certain of the characteristics of chronic dysentery. According to Sir Patrick Manson, it may be primary or secondary to other infections, notably to chronic dysentery. It is characterised by irregular alternations of exacerbation and comparative quiescence of symptoms, by erosive and inflammatory lesions of the tongue, mouth, and pharynx—very painful erosions, causing abundant salivation; by dyspepsia, usually very severe, accompanied by abdominal tympanism, borborygmi and vomiting, with or without nausea; by the evacuation of discoloured stools, which are extraordinarily abundant, frothy and fetid, without tenesmus, and without mucous discharges or blood; by extreme emaciation, anæmia, and a tendency to relapse on the occasion of the slightest exciting cause (exertion, or a chill, or a slight departure from diet, etc.).

All these specific symptoms will, as a rule, enable the physician to make a diagnosis.

Cases of amœbic dysentery, associated with cholera (Yakimov and Damidov) and with typhoid fever or typhus, have been reported, particularly in time of war. Laboratory research alone can enable one to arrive at a correct diagnosis in such cases.

Subcutaneous injections of salts of mercury and the ingestion, voluntary or otherwise, of certain berries (notably that of one of the *Euphorbiaceæ*, *Hura crepitans*) may simulate a dysenteric attack (Pierre).

II. Diagnosis of the Nature of Dysentery

In the presence of a plainly characterised dysenteric syndrome, one should always be able to determine its cause. *Clinical examination* by itself will set one on the right road. Bacillary dysentery, it will be remembered, often develops, in cases of average or extreme gravity, with a more or less elevated temperature, although this is not constantly the case, while amœbic dysentery is generally apyretic, except when complications are present. The chronic development of the disease and the knowledge that it is epidemic (in hot countries) enables us to form certain presumptions, but bacteriological examination is always necessary.

Sero-diagnosis may be useful. The serum of patients suffering from bacillary dysentery habitually agglutinates the dysentery bacillus which has caused the intestinal infection, but it agglutinates no other bacillus. In cases of medium or extreme severity, the agglutination does not appear until about the eighth or tenth day of the disease. It lasts as long as the disease lasts, is observed during convalescence, and often persists until two or three months after recovery. The agglutination index varies from $\frac{1}{20}$ to $\frac{1}{400}$. In slight forms of dysentery agglutination is, as a rule, absent, for such cases recover before the agglutinative power of the serum can make its appearance. If they are prolonged it may appear, even in cases of simple diarrhœa occurring during an epidemic, side by side with well-defined attacks of dysentery (Braun, Job, Dopter).

In cases of mixed infection by dysenteric amœbæ and bacilli, the agglutinative power of the serum may appear under ordinary conditions.

The following table summarises the chief differential characteristics of amœbic dysentery and bacillary dysentery.

Amœbic Dysentery	Bacillary Dysentery
Etiology	
Pathogenic amœba, inoculable into the rectum of cats.	Dysentery bacilli.
Usual Methods of Propagation	
More particularly, drinking water. Direct contagion. Contagion by encysted forms.	Direct contagion. Indirect contagion, from stools (latrines), flies, vegetables, infected soil, manure, dust, drinking water.
Epidemiology	
A disease of hot or tropical countries, where it is endemic. Prevalent in summer and winter. Indo-China, Tonkin, Saigon, United States, Brazil, Philippine Islands, Cuba, South America, Madagascar, Egypt, Sudan, Senegal, Morocco [India], etc.	A disease prevailing chiefly in summer and in temperate countries; less frequent in hot or tropical countries. Occasionally sporadic. Usually epidemic, spreading rapidly, and highly contagious. Prevalent in late summer and autumn.
Clinical Symptoms	
Tendency to chronicity. Immunity does not result from a previous attack. Hepatic abscesses are frequent. Serum does not agglutinate dysentery bacilli. Alkaline evacuations. Eosinophilia [sometimes].	Onset sudden, development acute, sometimes chronic. Previous attack confers immunity. No hepatic suppuration. Serum agglutinates dysentery bacilli. The dejecta are acid or neutral. Eosinophilia absent.
Anatomical Lesions	
Deep lesions often occur; ragged ulcers with detached [undermined] edges, localised in the large intestine.	Lesions extending over the whole of the large intestine, and often to the lower portion of the ileum. *Superficial lesions*: Yellow or greyish erosive spots, with hyperæmia of the mucous membranes.

An early and exact diagnosis can be established only by means of a simultaneous search for the incriminated parasites in the stools. In all cases of dysentery, there-

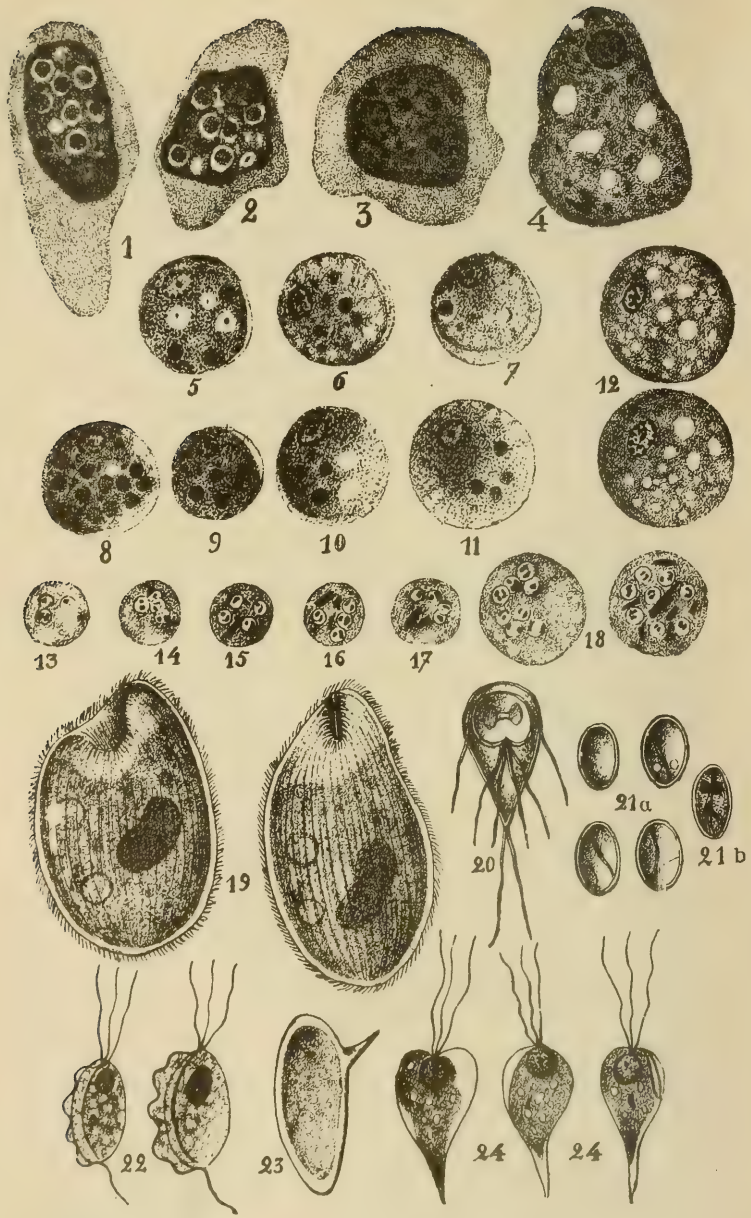
fore, a certain amount of systematic research must be undertaken in the laboratory.

Laboratory Research.—These investigations will comprise microscopic investigations with and without staining and cultivation. The former will permit of the cytological examination of the mucous discharges, and the discovery of amœbæ or amœbic cysts ; the latter will enable the investigator to isolate and identify the dysentery bacilli and the germs which may be associated with them.

Microscopic examination should deal with fæces very recently passed. By means of spreading and separating, smears may be taken from the most purulent portions of the mucous discharges. These smears may be fixed and coloured by the ordinary cytological methods (fixation by alcohol and ether, stained with thionin and eosin, hematein and eosin, Giemsa's stain, etc.). In the case of bacillary dysentery the preparations will show very large numbers of neutrophile polymorphonuclear leucocytes, normal or but slightly abnormal mononuclear leucocytes, and a varying number of bacilli.

In amœbic dysentery the preparations of mucus should be examined in the fresh state, between slide and cover-glass, taking care not to crush them unduly. Far fewer polymorphonuclear leucocytes occur than in bacillary dysentery, but they are greatly altered ; eosinophile leucocytes are sometimes found among them in considerable numbers, and the preparations are very rich in various bacteria, infusoria, etc. The number of these various elements is such that even if we do not meet with amœbæ we may sometimes presume the diagnosis to be that of amœbic dysentery. Only the discovery of amœbæ or their cysts can establish the diagnosis with certainty however.

Certain writers advise the passing of the stools into warmed vessels. H. Vincent has ascertained that the amœbæ remain motile for ten to thirty minutes, sometimes for an hour even, at the temperature of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Explanation of the Plate

1, 2, 3.—Living dysentery amœbæ. [*E. histolytica.*]

4.—Non-pathogenic living amœbæ. [*E. coli.*]

5, 6, 7, 8, 9, 10, 11.—Dysentery amœbæ. Stained with iron hematoxylin (from a preparation by Dr Langeron).

12.—Non-pathogenic amœbæ. Stained by iron hæmatoxylin.

13, 14, 15, 16, 17.—Cysts of dysentery amœbæ [*E. histolytica*] with four nuclei; 15, 16, 17, containing chromatoids.

18.—Cysts of non-pathogenic amœbæ with eight nuclei [*E. coli.*] One of these cysts contains chromatoids.

19.—*Balantidium coli.*

20.—*Lamblia* [Giardia] *intestinalis.*

21a.—Cysts of *Lamblid intestinalis.*

21b.—Cysts of *Lamblia intestinalis.* Stained with iron hæmatoxylin.

22.—*Trichomonas intestinalis.*

23.—Egg of *Schistosoma mansoni.*

24.—*Tetramitus* [*Chilomastix*] *mesnili.*

specific amœba of dysentery by the name of *Amœba coli dysenteriæ*, or that of *Entamœba*, the latter being proposed by Councilman and Lafleur. *E. histolytica* and *E. tetragena* are to-day regarded as phases of *E. dysenteriæ* (Job and Hirtzmann, C. Mathis and L. Mercier, etc.), not as distinct species.

In Morocco Job and Hirtzmann have usually found the *E. tetragena* at the moment of the dysenteric crisis. It is this type also—long regarded as more peculiar to African regions—which has been reported in France by Ravaut and Krolunitsky.

The *E. histolytica* type is characterised by its extremely active movements—so active that one cannot always draw the contours of the transparent chamber. It emits pseudopodia in considerable numbers, which are rapidly protruded and withdrawn.

The endoplasm, a greenish-yellow, is crammed with cellular and alimentary debris, and especially with red corpuscles.

It also contains bacteria, and, more rarely, chromatoid bodies.

The ectoplasm is transparent and refractile.

The living amœba appears to be without a nucleus, but when its movements become less rapid, or cease, the nucleus appears, round, and provided with a nucleolus. The endoplasm and the ectoplasm seem less differentiated, and one can plainly recognise the red corpuscles or their debris.

In fixed and stained preparations *E. histolytica* appears round, confined by a clear outline, and containing numerous vacuoles which enclose red corpuscles; the nucleus appears round and excentric, with a peripheral ring of chromatin granules and a single centriole.

E. tetragena[1] is found only in the fæcal evacuations (Ravaut and Krolunitsky). Its movements are much less rapid than those of the amœba just mentioned,

[1] The small forms found in the fæces are usually spoken of as the *E. minuta* type by English authorities; they are generally regarded as the immediate precursors of the cysts.—Ed.

the endoplasm and the ectoplasm are less distinct, the red corpuscles included are less numerous, and the nucleus is very apparent.

In the immobile condition it is hardly to be distinguished from *E. histolytica* when the latter has become immobile.

In addition to the pathogenic amœba one very often meets with another, *E. coli*, which is regarded as normal to the colon. Its movements are very slow, the endoplasm and the ectoplasm are poorly differentiated, the nucleus is very plainly visible, and it encloses no red corpuscles.

In fixed and stained preparations the nucleus presents the same structure as in *E. dysenteriæ*, but there are generally several centrioles.

The living amœbæ are easily recognisable, but when the stools are examined some hours after being passed, they have become immobile. It is then more prudent to search for the cysts. While the amœbæ are found in the living condition only during crises the cysts are [may be.—Ed.] visible during the whole course of the disease. They are sought for by direct examination, between slide and cover-glass, with or without coloration. According to Langeron, the addition of a little Lugol's solution to the preparation notably facilitates the examination. C. Mathis fixes fresh, undried preparations by exposure to the vapour of osmic acid (1 per cent.) for thirty seconds. He then stains, for a few seconds, with hæmatoxylin (1 in 200). The envelop and the nuclei of the cysts are stained a deep brown, thus becoming plainly visible.

To identify the cysts we must note their dimensions and the number of their nuclei.

The cysts of *Entamœba dysenteriæ* [*E. histolytica* of English authors—Ed.] measure at most 10–14 μ in diameter, and possess 1 to 4 nuclei, never more (E. Job and L. Hirtzmann). In the protoplasm one very often sees agglomerations of a refracting substance, which occurs in thick rod-like bodies or irregular masses; it is

known as chromidium, and according to C. Mathis is characteristic of this variety of cysts.

The cysts of *E. coli* (non-pathogenic) measure 16–25 μ and even more; they possess 1 to 8 nuclei. The cysts of *E. dysenteriæ* [*E. histolytica*], like those of the non-pathogenic amœba, may or may not contain chromatoid bodies.

For purposes of diagnosis one should observe only the ripe cysts—that is, those containing 4 and 8 nuclei.

The number of cysts is very variable; sometimes very abundant in each preparation, they are, on the contrary, very rare in other cases. Ravaut and Krolunitsky facilitate their elimination by the artificial production of a temporary attack of enteritis, either by means of a saline purgative or a saline enema, or, better still, by the intravenous injection of 1 to 4 centigrammes of cyanide of mercury.

Noc, with the same object in view, administers an enema of boiled water (500 c.c.). When this has taken effect he employs an irrigation or instillation, lasting thirty minutes, with $\frac{1}{2}$ per cent. solution of thymol (in boiled water).

A. Mauté administers, in the morning, an irrigation with:

Iodine	1 gramme
Iodide of potassium	2 grammes
Water	1 litre

The amœbæ and cysts are looked for in the diarrhœal, or merely soft, or sometimes even formed stools, which the patient passes during the evening or the next morning.

The cysts remain intact in the stools for at least two days. If the investigation has to be undertaken later than this, the addition of formol will preserve them perfectly.

Mauté attaches very great practical importance to the investigation of associated parasites, the super-

addition of these seeming to maintain and augment the resistance of the amœbæ.

One should, according to him, look for protozoa (the trichomonas especially) and intestinal worms (ascaris, trichocephalus, etc.).

The final disappearance of cysts in the stools is the only criterion which we at present possess of recovery from amœbic dysentery.

The bacteriological diagnosis of bacillary dysentery necessitates the culture and isolation of the bacillus, as well as its identification.

1. Culture. Isolation.—A flake of mucous or muco-purulent matter is washed several times in sterile bouillon or physiological serum, in order to free it of gross impurities.

The culture is then made on several Petri's dishes, into which some litmus lactose agar, and also Endo's agar, has been poured. The agar is inoculated by spreading the flake of mucus on it and moving it gently to and fro by means of a platinum wire or a bent glass rod. After twenty-four hours in the incubator, at a temperature of 37° C., the inoculated portions are examined. On the agar containing litmus, red and blue colonies will be found; on the Endo's medium some red colonies will be seen, and others which are colourless. The red colonies are eliminated; it is in the blue and colourless colonies that the dysentery bacilli will be found.

2. Identification.—The dysentery bacillus is a short rod-shaped bacillus, rounded at its extremities, easily absorbing all the aniline stains, but negative to Gram's stain. It does not form spores, but shows polar granulations. Its movements are feeble, confined as a rule to slight oscillations like those of a compass-needle settling to the north. This motility, which Flexner observed in his bacillus, is very slight even in the case of recent cultures made directly from dysenteric stools; in sub-cultures it progressively diminishes, finally disappearing.

PRINCIPAL DIFFERENTIAL CHARACTERISTICS OF THE FOUR TYPES OF DYSENTERIC BACILLI

BACILLUS	SHIGA	FLEXNER	HIS (Y)	STRONG
Production of indol	No indol	Indol	Indol	Indol
Litmus milk	Reddens very slightly: turns amethyst after twenty-four hours	Reddens more perceptibly than Shiga's	As Flexner's	As Flexner's
Neutral red media	No change	No change	No change	No change
Litmus agar and dulcite, litmus agar and lactose	No fermentation	No fermentation	No fermentation	No fermentation
Litmus agar and glucose, litmus agar and galactose, litmus agar and lævulose	Turns red	Turns red	Turns red	Turns red
Litmus agar and mannite, litmus agar and raffinose	No fermentation	Turns red	Turns red	Turns red
Litmus agar and maltose	Turns an inconstant red after several days	Turns red	Red tinge obtained rarely and with difficulty	Change to red capricious and slow
Agglutination	With Shiga serum only	Agglutination with the Flexner and Y serums, but not with Shiga and Strong serums	Same as Flexner's	Agglutinated only by Strong serum
Experimental pathogenic action	Subcutaneous injection produces dysentery in the rabbit, dog, rat, and mouse, but not in the guinea-pig	Subcutaneous injection produces no pathogenic results. Injected under the peritoneum it produces fatal peritonitis in the guinea-pig, rat, and mouse	Same as Flexner's	Same as Flexner's

According to Sir Patrick Manson, Shiga's bacillus displays two to six terminal flagella, rather short and thick; those of Flexner's bacillus are said to be longer.

The dysentery bacillus does not coagulate milk; on gelatine the isolated cultures are shallow and translucid, their edges being "pinked," while they are crossed by furrows which give them the appearance of vine-leaves.

There are races of dysenteric bacilli, just as there are races of cholera vibrios and typhoid bacilli. These races comprise types which are steadily increasing in number. At the present time there are only four races which present characteristics definite enough to enable us, whenever a germ is isolated, to refer it to one of them for identification. Between these four types there are a great number of varieties which are more or less differentiated one from another.

In addition to these we also encounter a certain number of so-called pseudo-dysentery bacilli, which, by their histological characteristics and their reactions are more or less differentiated from the true dysentery bacilli.

The table given on p.322 summarises the essential characteristics of the four principal types.

CHAPTER III

THE TREATMENT OF DYSENTERY

The diagnosis of dysentery being established, the patient should immediately be put to bed and kept warm, and as far as possible be prevented from leaving his bed, even to visit the commode. The alimentary canal should be kept in a state of repose.

All solid food must be suppressed. Foods must be selected which, while possessing high nutritive qualities, leave a minimum of fæcal residue. Milk, beef-tea, white of egg, barley water or rice water, and peptonised milk should constitute the basis of alimentation (Manson).

Vegetable bouillon, which has yielded such good results in the treatment of diarrhœa in children, has been employed with success by Boudet. To assuage thirst, weak lukewarm tea is welcomed by the patient.

Alcohol and alcoholic beverages are only to be given in cases where collapse is to be feared.

Liquid nourishment, more or less abundant according to the case, and at times bordering upon full diet, should be continued until the stools are no longer numerous, and simply diarrhœal. At this stage one may give very light *purées* of dry vegetables or potatoes. Meat diet is to be resumed only with the utmost prudence.

Treatment must be subordinate to the diagnosis given by the laboratory. Some of the various cases which may present themselves will now be considered.

1. In Cases of Bacillary Dysentery.—We now have a specific treatment for this form of dysentery. Shiga, in Japan, in 1898, was the first to utilise the curative

properties of the serum of animals immunised against the dysentery bacillus. Simultaneously Rosenthal and Gabritchevski in Moscow, Vaillard and Dopter, and Auche and Coyne in France were undertaking investigations of the same nature. Vaillard and Dopter, by weekly inoculations of living cultures of dysentery bacilli into the veins of the horse, obtained a serum which possesses preventive and curative effects in cases of experimental dysentery in animals.

Injected into the human sufferer from bacillary dysentery this serum diminishes mortality, attenuating and causing the rapid disappearance of the dysenteric phenomena. A few hours after the injection of the serum the patient usually experiences a genuine feeling of improvement, the abdominal pains, the tenesmus and the straining already abating, and, except in very serious cases, they almost always disappear during the ensuing twenty-four hours. Recovery takes place in forty-eight hours, five or six days or ten to fifteen days, accordingly as the case is slight, average, severe, or very severe. Convalescence is shorter and easier. The serum is given by subcutaneous injections. Its effects are more rapid and decisive in proportion as it is administered more promptly after the onset of the disease. The dose varies according to the moment of intervention, the severity of the attack, and the age of the patient. The following indications are given by the inventors of the serum treatment: For adults in dysentery of average severity, taken at the outset, 20 c.c. will usually suffice to produce an immediate arrest of all the symptoms. If these still persist after the lapse of twenty-four hours, another injection of 20 c.c. should be given. In severe forms, or cases of several days' standing, a third injection of 10 c.c. will be useful.

In serious cases 40 to 60 c.c. should be injected at once, and the physician should not hesitate to repeat the injection daily, even to the length of administering a dose of 100 c.c. per diem, in two injections, until

the intestinal disturbances abate. The treatment is then carefully continued, with diminishing doses, until the number of stools falls to a few in the course of the twenty-four hours.

For children the above doses are to be reduced by one-half, two-thirds, or three-quarters, according to age.

In certain cases which are refractory to serotherapy, and in chronic forms, enemas of serum, reaching as high a point of the colon as possible, have been recommended.

Medical treatment by means of Segond's pills (*vide*, p. 329) (2 to 6 per diem), or by sulphate of sodium (10 grammes per diem), together with opium, leads to a quick recovery in dysenteries of average severity, in default of the serum treatment.

2. In Cases of Amœbic Dysentery.—Hydrochloride of emetin is at present regarded as the most active remedy in the treatment of amœbic dysentery, but although it acts rapidly on the inter-organic amœbæ lodged in the liver or the walls of the intestine, it has no action on the extra-organic amœbæ—that is, those which are free in the intestine. Moreover, the treatment is often followed by relapse. It has been proposed to continue the treatment by subcutaneous injections (Chauffard) and also to complete the cure by injection by means of local treatment (irrigations) which would reach the amœbæ remaining in the intestine, but this latter treatment is usually ineffectual.

Certain writers give two intravenous injections of 0·15 to 0·20 grammes of hydrochloride of emetin in 100 c.c. of physiological serum, and then, during a period of one or two weeks, subcutaneous injections of 0·10 to 0·12 grammes. Lastly, supplementary cures are administered every three or four weeks. The dejecta are examined periodically for some months with a view to the discovery of amœbic cysts, after an iodated enema.

Mauté, during the first three or four days, gives two

subcutaneous injections of hydrochloride of emetin, the dose being 4 centigrammes per injection; then, during the three or four subsequent days, he gives a single injection.

Generally speaking, the dysenteric phase is then over, and the patient no longer passes more than one or two stools in the day. If, on the contrary, the diarrhœa persists, one should suspect parasitic associations, and should look for them and treat them (with worm-seed, santonin, thymol, turpentine, etc., according to the case).

Mauté then gives five series of five injections, each leaving an interval of a week between each series. If after the administration of an iodated lavage he discovers no more cysts in the stools, he regards the patient as cured. Despite these long series of injections, however, it often happens that one still discovers evidence of amœbic development.

In these cases, following the method of Ravaut and Krolunitsky, Mauté employs novarsenobenzol. Every six or seven days he gives an injection of ·15, ·30, ·45, ·60, to ·75 grammes. If cysts are still found in the stools a few days after the end of the treatment, he gives two series of five injections each of emetin (two injections of 8 centigrammes and three of 4 centigrammes), each series following the preceding series at an interval of eight days. About 6 per cent. of dysenteric subjects are still infected after this treatment. Mauté is of opinion that it is to the interest of such patients to continue the treatment by emetin and novarsenobenzol.

This is also the opinion of Milian, who employs hydrochloride of emetin and "606" concurrently; of Ravaut and Krolunitsky, who employ arsenobenzol, and of Noc, who employs "914," which he regards as a remedy of great utility in improving the general condition, superior to the ordinary arsenical compounds.

Despite its incontestable value, hydrochloride of emetin does not always succeed. It has little or no

effect on the cysts.[1] In the chronic and refractory forms of amœbic dysentery the physician may profitably resort to the treatment indicated on p. 330

3. In Cases of Mixed Dysentery, Bacillary and Amœbic.— The physician will successively administer injections of hydrochloride of emetin and of anti-dysenteric serum, and will be guided by the indications already given.

4. (*a*) **When the Results of Examination in the Laboratory are Negative.** — Reserving treatment by emetin and serum for serious cases, the physician may resort to the older remedies. There are a certain number of remedies which gave proof of their value in the days when etiological diagnosis was unknown. These remedies may be recommended either as auxiliary to the treatments reputed to be specific, or in cases where, for whatever reason, the physician cannot or does not wish to employ the specific treatment. These are: ipecacuanha, the saline purgatives, calomel, and opium.

Ipecacuanha may be administered in several ways: alone, or in association with other drugs, notably with calomel and opium. Alone, it is given in fractional doses, according to the so-called Brazilian method. It is prepared and administered as follows:—250 grammes of boiling water are poured upon 4 to 8 grammes of the powdered root; this is left undisturbed for twelve hours, then decanted; in the same way a second and a third infusion is made, followed by maceration.

Each of these infusions is taken per day, at the rate of a spoonful every hour. The first infusion sometimes

[1] Recent researches have shown that a large proportion of cases treated by emetine hydrochloride relapse and become chronic cyst carriers. Oral administration of emetine, in the form of Emetine bismuth iodide grs. iij. nightly for twelve nights—*e.g.* 36 grains in a course—has been found to be much more efficacious in sterilising cases, and recent reports by Dobell claim 80 to 90 per cent. of cures by this method. Alcresta ipecacuanha has also been tried by Stephens, and Wenyon suggests a combined oral and hypodermic treatment with emetine hydrochloride.—Ed.

causes vomiting, and often numerous stools. The second rarely produces vomiting, but more frequently nausea; it does not perceptibly affect the number of stools. The third, as a rule, produces no incidental effects.

Saline purgatives, sulphate of sodium in particular, are in current use. They may be administered until the stools contain no more mucus and have become fæcal. The treatment commences with 30 grammes of sulphate of sodium, progressively diminishing doses being given day by day, or small doses of 5 to 10 grammes may be administered, repeated several times in the day, until the purgative effect is produced, or 15 grammes may be given for the first two days, and 10 grammes the third and fourth days.

Segond's pills may be tried, their composition being as follows:

Ipecacuanha (pulv.) . . .	0·05 grammes
Calomel	0·02 ,,
Extract of opium	0·01 ,,
White honey *q.s.*	

To make one pill

These pills should be recently prepared. They are very efficacious. Four to six are to be given daily, the number being steadily diminished as the stools improve. Their employment should be discontinued immediately appearances of stomatitis set in.

Calomel has often been employed alone also, the daily dose being 1 gramme to 1 gramme ·20, or doses of 30 centigrammes are administered every six or eight hours, or fractional doses hourly. The doses are diminished and the intervals between them increased when improvement is obtained. Mercurial stomatitis is of frequent occurrence after such treatment.

Opium, by itself, should be employed with reserve, and only as a temporary remedy.

Suppositories of cocaine or morphia ease the tenesmus. Belladonna calms the pains without producing constipation, and may therefore be employed, but with

prudence. Kho-sam, the oleaginous seeds of *Brucea sumatrana*, is said to cause the rapid disappearance of dysenteric phenomena (Mougeot, Lemoine).

4. (*b*) **In Cases of Chronic Dysentery.**—First of all a purgative should be given (calomel or sulphate of sodium).

The systematic employment of Segond's pills or of sulphate of sodium (10 grammes in the morning) yields good results. It is necessary, however, to supplement these by medicinal enemata.

Manson recommends a brief preliminary treatment with ipecacuanha, preceding the administration of castor oil.

To produce an alternative effect on the ulcerated intestinal surfaces, local dressings have been proposed.

Guido Izar examines the rectum and the sigmoid colon directly, with the aid of an instrument constructed by Melocchi, which bears the name of the recto-sigmoidoscope, and which is a happy modification of the endoscope of Desormeaux. He then applies dressings directly to the dysenteric ulcerations, painting them with a 2 per cent. solution of permanganate of potassium, or a 1 per cent. solution of nitrate of silver, or oxygenated water, or powdering them with dermatol, or a mixture of charcoal and kaolin, according to Ascoli's method. It is manifest that this treatment can only be applied to ulcerations confined to the lower portion of the large intestine. It cannot, therefore, be employed in all cases.

Intestinal irrigations or enemata may be administered —a solution of nitrate of silver, 0·5 per 1000, boric acid, 20 per 1000 (Le Dantec), permanganate of potash, 0·5 per 1000 (Gastinel), oxygenated water containing ten times its volume of oxygen diluted with five times its volume of tepid sterilised water (Rocaz), tincture of iodine, 1 per 1000, sulphate of copper, and creosote, 1 or 2 per cent. (Zanardini). These latter are toxic, however, owing to absorption in the region of the ulcerations.

Le Dantec also employs what he calls an irrigation dressing, always preceded by a cleansing irrigation. He employs sub-nitrate of bismuth, 20 grammes to the dose, the bismuth being in suspension in a litre of tepid water ; or else the following mixture :—

Dermatol	20 grammes
Bicarbonate of soda	2 ,,
Water	1 litre

The most effectual disinfection for rapidly accomplishing the destruction of the amœbæ and their cysts is obtained by the following enema (H. Vincent), preceded by a detergent intestinal irrigation with physiological water (lukewarm) :—

Labarraque's Solution	10 to 12 grammes
Nacl	5 ,,
Distilled water	1000 ,,

These enemata may be given daily, drop by drop (by the *goutte à goutte* method), without pressure, the patient retaining them as long as possible. At first, 20 to 30 drops of tincture of opium may be added.

The enema should be given warm (98·4° to 104° F.), very slowly, with the long rectal tube, the patient lying on his right side.

At the same time the patient is given 6 to 10 grammes of sulphate of soda each morning, and during the day a draught consisting of :

Syrup of ipecacuanha	5 to 6 grammes
Extract of opium	0·05 to 0·10 ,,
Water	120 ,,

a spoonful being given every two hours, no liquid nourishment is to be taken within thirty minutes of taking the dose.

Warming the abdomen by means of the electric apparatus of Laroquette greatly assuages the colics.

The preceding treatments sometimes give rapid recoveries from amœbic dysentery.

In patients suffering from chronic dysenteries of amœbic origin, who frequently suffer from malaria as well, the physician must never neglect *the simultaneous administration of quinine*, preferably by subcutaneous injection. Malarial attacks, even when slight or attenuated, very often cause returns of amœbic dysentery in tropical patients.

PART II.—THE EPIDEMIOLOGY AND PROPHYLAXIS OF DYSENTERY

As has been noted in the foregoing chapters, dysentery is a *syndrome* common to several infections. If by dysentery we understand the contagious process characterised by the painful and repeated emission of bloody and mucous stools, determined by the lodgment of a parasite in the large intestine (and sometimes in a portion of the small intestine), we must include, under this heading :

1. Bacillary dysentery.
2. Amœbic dysentery.
3. The dysenteries due to *Balantidium coli*, *Trichomonas intestinalis*, and *Schistosoma mansoni* ; and, lastly, other forms as well, of a more exceptional kind, such as the dysenteries due to spirilla, to *Chilodon dentatus*, to Leishmaniasis, etc.

The etiological conditions which govern each of these dysenteries are subordinated to the biological characters of their pathogenic germs, their degree of resistance in the external environment, and the degree to which desiccation, the oxygen of the air, light, etc., are able to affect them.

All these dysenteries, which in reality differ greatly from one another, none the less possess, when considered from the epidemiological standpoint, a number of fundamental characteristics which form a common link—namely, the fact that their infectious agent vegetates in the lower portions of the alimentary canal ; that it propagates itself in the mucous membranes, the glandular tissue, and the tunicæ of the intestine ; that it provokes ulcerative lesions there ; that it is eliminated in profuse quantities with the repeated

dejecta of the patient ; and, finally, that the pathogenic agent residing exclusively or principally in the fæces always constitutes, whether directly or indirectly, the fundamental agent of contagion.

From our knowledge of the plurality of dysenteries it results that, when considered as a whole, the epidemiological rules of these fundamentally different maladies none the less offer a large number of common features. In reality, however, there are two of these various forms of dysentery which, owing to their frequency and their gravity, greatly predominate over all the rest—namely, bacillary dysentery and amœbic dysentery.

These two affections, then, from the epidemiological point of view, as from the clinical standpoint, are those which should more particularly receive our attention. We shall consider them, therefore, in succession.

CHAPTER IV

EPIDEMIOLOGY OF BACILLARY DYSENTERY

Bacillary dysentery is caused by a special bacillus seen by Chantemesse and Widal, and described in a specific manner by Shiga, then by Kruse, Flexner, Strong and Musgrave, Rosenthal, etc., etc., and finally by L. Rogers, Vedder and Duval, Dopter and Vaillard, etc. It constitutes, in reality, one species of syndrome resulting from different *races* of the same microbe. At least four groups of these are recognised (see Part I.), excluding the pseudo-dysentery bacilli, which react in a specific manner in the presence of sugars and form, or do not form, indol, and whose other biological characters (agglutination, bacteriolysis, and the specific action of immunising serums) are more or less distinct. We have already discussed these groups.

Bacillary dysentery is a ubiquitous malady. We find it in all countries, in all climates, but it is especially a malady of cold or temperate countries. In this respect it is unlike amœbic dysentery, which is more common in hot climates.

On the other hand, each epidemic of bacillary dysentery seems to possess its own variety of microbe (Shiga). The bacillus of the type discovered by Shiga was isolated in Korea, in the Japanese army, as well as in Manchuria, and also in Russian soldiers at Port Arthur and the sailors of the Baltic squadron.

At the time of the Tokio epidemic this original bacillus was extremely rare, and the bacilli encountered were those of the other races.

In the Kobe epidemic of 1906 Amako found Shiga's bacillus, or its varieties, in all the invaded quarters.

At the end of the epidemic only the varieties were found.

Shiga's bacillus is regarded as the most dangerous, but Flexner's may give rise to very severe forms of dysentery.

Epidemics due to bacilli of the Flexner type are common in the Philippines, the United States, and Porto Rico; the same bacillus is found, however, in epidemics in Central Europe, France, Tunisia (Nicolle and Cathoire), Russia, Algeria, Morocco, India, etc.

In some epidemics bacilli of several races may be found (the Shiga type, the Flexner type, the Y type, etc.).[1]

In Delhi dysentery due to the Y bacillus is predominant (Kurnen).

In Paris the bacilli isolated are sometimes of the Shiga type, sometimes of the Strong or Flexner types.

During the present war certain epidemics have been reported in Galicia and Russian Poland, in which bacteriological examination has in the great majority of cases failed to isolate the germ. In the examination of more than 1000 stools Shiga's bacillus was isolated only six times, Flexner's twice, and the Y bacillus once, nothing being found in the other cases.

Generally speaking, bacillary dysentery is prevalent everywhere in Europe, but more particularly in the Mediterranean basin (Greece, Turkey, Italy, Sicily, Spain, Gibraltar, and Catalonia).

Certain countries, as the north of Italy, for instance, are sometimes visited by serious epidemics of bacillary dysentery. Celli has described the epidemic of Belluno, where, in 1894, out of 5700 inhabitants, 2564 were attacked. Galli-Valerio has published an account of the epidemic in the Valtellina (1897), in which the mortality amounted in certain localities to 20 per cent. of those attacked. In Switzerland a serious epidemic visited Leuk, in 1893; it lasted three months, with a mortality of 25 per cent.

[1] Morgan's type was also found in cases of dysentery at the Dardanelles.—Ed.

Armand Ruffer and Wilmer have mentioned the serious epidemics of bacillary dysentery which occur among pilgrims who have returned from Mecca. It is estimated that in the vilayet of Hedjaz this malady causes 1000 to 15,000 deaths annually.

The epidemics of dysentery observed in our armies at the front during the present war against Germany have, as a rule, revealed the bacillus of the Flexner type, more rarely the Y type (Bonnel, Joltrain, and Taufflieb), but Shiga's bacillus has also been isolated.

Each of these microbes may therefore give rise to epidemic patches, more or less distinct and of greater or less extent, which may run into one another.

German writers (Kruse and Doerr) are wrong in attributing epidemic dysentery to Shiga's type alone (the other bacilli being said to give rise only to sporadic pseudo-dysenteries). This differentiation is invalid. Neither can we admit the existence of a dysentery special to children and lunatics, as Kruse would have it. As a matter of fact, we may find Shiga's or Flexner's bacillus indifferently (Auché).

In France there is an important endemic centre in the departments of Brittany, where certain arrondissements have formerly suffered as many as 500 deaths. Dysentery is also found in Champagne, and in the Basse Somme and in the eastern division of France.

The official statistics published by the Ministry of the Interior do not give figures relating to the precise frequency of dysentery in France, as the disease is not subject to compulsory notification.

Dysentery in Armies

The sanitary condition of the army is in general in close relation to that of the civil population. The frequency of dysentery in military circles is, therefore, in accordance with the epidemic or endemic conditions of the garrison towns. It is important to note, however, that the soldier is particularly vulnerable. The

statistics of the French Army refer, as a rule, to the sum of the various dysenteries: bacillary, amœbic, etc. It may be affirmed, however, that in France, in time of peace, bacillary dysentery is almost the only form to be met with, excepting a few imported cases of amœbic dysentery, the subjects being colonial soldiers. The average frequency of cases hovers about 1 per 1000, rather below this figure than above it. The region of Lyons is that most affected. Then follow the 18th Army Corps (Bordeaux), the 13th (Clermont-Ferrand), the 10th (Rennes), the Military Government of Paris, the 15th Army Corps (Marseilles) and the 20th.

The Tunis and Oran divisions and the troops in Morocco reveal a morbidity and a mortality which are uniformly higher. But to the cases properly referable to regional influences we must add the numerous cases which are explained by the fact that dysenteric soldiers are sent home from Tonkin, Madagascar, Senegal, etc.: countries in which dysentery is endemic.

The two forms of dysentery, bacillary and amœbic, are found to co-exist in the French possessions in North Africa.

The statistical records of the French Army reveal rather a high proportion of cases, which is due to the fact that they represent the total number of cases reported in Tunis and Algeria as well as in France.

Of all armies that of the United States is most subject to dysentery.

In the French Army the severest forms of bacillary dysentery are observed, as a rule, among the troops in Algeria and Tunis. Certain epidemics (Hussein-Dey, 1894) have been extremely formidable, owing to the frequency of hypertoxic forms with hypothermia and a rapidly fatal termination.

At intervals, for that matter, there have been epidemics of equal gravity in France. G. Bertillon has recorded an epidemic which broke out in July, 1915, in a squadron of dragoons, which yielded 12 cases, of which 5 were of an extremely grave character.

Dysentery shares with typhoid fever and the paratyphoid fevers the peculiarity of attacking armies in the field. It is, however, less frequent than these. It is in a way inseparable from the medical history of

DYSENTERY IN THE WORLD'S ARMIES

Morbidity per 1000 Men

ARMY	1903	1904	1905	1906	1907
French	2·34	2·27	1·66	2·38	1·08
German	0·17	0·03	0·10	0·30	0·01
United States	37·71	22·49	16·93	14·47	
British	0·80	0·60	0·40	0·40	0·50
Austrian	0·50	0·50	0·60	0·50	0·40
Bavarian	0	0	0	0·06	0·02
Belgian	0·07	0	0	0·03	0·06
Spanish	0·27	0·12	0·07	0·05	0·10
Italian	0·30	0·50			
Dutch	0·10	0			
Russian	0·90	0·50	0·70	0·90	0·70
Rumanian	0·65	0·90	2·90	0·60	0·70

warfare. In 1415 the English Army, which had invaded France, became the prey of a terrible epidemic. After the battle of Agincourt it had to be repatriated, having lost three-fourths of its effectives.

Pringle has recorded the epidemic which raged through the English Army in July, 1743, at Dettingen; half the soldiers were attacked. The War of the Polish Succession, the Austrian War, and the Seven Years' War were marked by epidemics no less deadly in character.

After the battle of Valmy the troops of the Coalition carried dysentery into Champagne. The Prussian Army, reduced to half its effectives, beat a retreat. At the time of the wars of the Revolution and the Empire, Desgenettes remarked that dysentery had very often killed more men than the fire of the enemy. In Egypt Napoleon lost 2468 men from dysentery.

It must be added that in those days dysentery was a disease of extreme gravity, such as is unknown in our time.

At the beginning of the conquest of Algeria dysentery caused as many deaths as malaria, and even more (Kelsch).

It was prevalent during the Crimean War. Between May and September, 1855, 9000 cases and 1478 deaths were reported. During the Italian War it was almost as common as typhoid and malaria.

The War of Secession shows how great the intensity of this malady may be on the occasion of great movements of troops. There were 238,812 cases of acute and 25,670 of chronic dysentery among the white troops, with 4804 and 3229 deaths respectively. These figures are very much less than the reality, for an enormous number of cases of acute diarrhœa were recorded (1,155,226), in addition to chronic cases (170,488), which altogether caused 30,481 deaths.

We shall see later that diarrhœa is very often only the abnormal or attenuated expression of dysenteric infection.

The German Army was much harassed by dysentery during the war of 1870–1871. There were 35,652 cases and 2380 deaths due to this malady. The troops besieging Metz had an enormous proportion of cases.

The Russo-Turkish War afforded another proof of the intensity of this disease in time of war. Cases of diarrhœa were extremely numerous, very few men escaping it. The statistics record, for the army of the Danube, 34,198 cases (57·75 per 1000) of dysentery, and 9543 deaths (16·11 per 1000). The army of the Caucasus, much weaker in numbers, was visited even more severely: 22,084 cases (90 per 1000) and 3552 deaths (15 per 1000).

During the short Bosnian Campaign the deaths from dysentery for a total effective of 198,000 men were 324.

During the Tunis Expedition among 20,000 men there were 3954 cases and 83 deaths from the same disease.

At the time of the Chino-Japanese War dysentery appeared as soon as the Japanese Army disembarked in Korea. Although the season was winter, the hospitals were overflowing with cases of dysentery. There were 12,052 cases among 200,000 men.

The French Expeditionary Corps sent to China at the time of the Allied Expedition in 1900 had 818 cases and 52 deaths. The American troops (1947 men) had 353 cases in two months.

Among the British troops sent to South Africa at the time of the Boer War there were more than 2500 cases of dysentery.

During the Russo-Japanese War the Russians had 6140 cases and the Japanese 6624 cases.

The Morocco Expeditionary Corps had 1080 cases of dysentery (amœbic) in 1912, and 1295 in 1913 (Job).

The war of 1914 has been no exception to the rule. Dysentery made its appearance among the soldiers of the French Army after the battle of the Marne. Since then it has been encountered continually in the various armies at the front, in France, at the Dardanelles, and at Salonika, sometimes appearing in grave and deadly forms, but more often in benign forms which lead to a prompt recovery.

Remlinger has reported this malady among the French troops in the Argonne. He isolated an atypical and not very toxic bacillus. L. Tribondeau and Fichet have published the results of their investigations as regards dysentery at the Dardanelles. The bacillus most frequently isolated was that of Shiga's type (23 times out of 38) ; the Y bacillus was found twice, and the bacillus of Morgan's type 13 times.

In 1915 a serious epidemic of dysentery appeared among the German armies in Galicia. The death-rate amounted to 16 per cent. of those attacked.

During all the epidemics which have appeared in France, in the civil population as well as in the armies, physicians have drawn attention to the frequency, sometimes excessive, of concomitant diarrhœa. At the

time of the epidemic which broke out at Versailles in 1902, in the 1st and 5th Regiments of Engineers, a fourth of the patients suffered from simple diarrhœa. It was the same in 1903 in the case of the 3rd Battalion of Chasseurs at Grenoble.

When the agglutinative reaction is sought for in such cases of simple diarrhœa, it is commonly found to be positive. Job, Braun, and Roussel have often verified this fact.

During the present war against Germany all physicians have noted the frequency of these diarrhœas, which, bacteriologically speaking, may be laid to the account of the dysentery bacillus (Sacquépée, Burnet, and Weissenbach).

Consequently, in addition to confirmed cases of dysentery, we must reckon with ill-defined or attenuated forms. From the epidemiological standpoint these are extremely important, as they lend themselves with great facility to the propagation of the disease by reason of the fact that, being apparently of little importance, they do not seem to necessitate any special precautions.

The chronic forms of bacillary dysentery, and the diarrhœa of children, which may also contain the bacillus in great profusion (Flexner and Strong, Vedder and Duval), are subject to the same remarks. Duval and Basset, during an epidemic, examined the stools of forty-two patients suffering from simple diarrhœa, and found the dysentery bacillus in them. Shiga has reported a similar experience.

Of course, all cases of diarrhœa observed in the armies in the field are not due to the dysentery bacillus. Many are due to infection by the enterococcus of Thiercelin, to the *Proteus vulgaris*, or to the polymicrobian vegetation which readily attains an unrestrained development in the case of overworked men. But the dysentery bacillus is incontestably responsible for a great number of those cases of common diarrhœa which are always encountered side by side with the classic dysenteries.

CHAPTER V

ETIOLOGY

The Predisposing Causes of Bacillary Dysentery

Bacillary dysentery exists in all countries and all climates, but, as we have already remarked, it is most commonly met with in cold and temperate countries.

When it appears in cold countries it gives rise with moderate frequency to serious epidemic manifestations. Sweden, Norway, the northern regions of Russia, Kamchatka, and Denmark have all been visited by epidemics, some of these being of great severity.

But the influence of cold climates is by no means absolute. Here is the proof: if we examine the curve of endemicity among the civil population or in the army in temperate climates, we find that it reaches its maximum, more often than not, during the hot season —that is, in the summer, and, above all, in the autumn.

During great wars, and notably during the present war, dysentery has evaded the influence of the hot season and has been prolonged into the winter. During the Crimean War the French trenches were full of men sick of dysentery during the coldest months of the year.

It was the same during the War of Secession. The months of November and December, 1862, were marked by a great recrudescence of dysentery.

Exposure to cold by day, and above all by night, under canvas and in the trenches, abdominal chills, and the effects of rain, which soaks men's clothes (Cambay), and the fording of rivers, which has the same result, have been invoked as predisposing causes.

Individual predisposing causes deserve mention. All ages are susceptible; nevertheless children seem to

be more often attacked in countries where the disease is endemic, as well as young people who have recently arrived in the country. This is often seen to be the case with young soldiers.

Neither are there any *races* which are refractory to this form of dysentery. It is as prevalent in the northern regions as in the south of Europe. The yellow race is as frequently attacked as the white race, nor does the black race escape.

Domestic animals, such as the dog, may contract bacillary dysentery, as has been proved by bacteriological examinations.

The predisposing influence of extreme *fatigue*, and of *over-exertion*, has justly been incriminated. Wars realise these conditions in the highest degree. It is the same with physiological poverty, a defective diet, coarse and indigestible food, the abuse of biscuits, etc. During the Balkan War the Russian doctors laid stress upon these different causes, notably the consumption of decomposing bread, putrefying food-stuffs, and impure water. To these one must add the inhalation of unwholesome emanations (from latrines, cess-pits, decomposing corpses, etc.), which cause, as in the diarrhœa of the operating theatre, an irritation of the mucous lining of the intestines, a hypersecretion of bile, and an eliminating diarrhœa ; this irritation prepares the ground for specific infection by the dysentery bacillus.

The protective effect of a *previous infection* is of great importance. It is well established that a first attack of bacillary dysentery confers substantial immunity, and this explains why, in countries where dysentery is endemic, it more particularly afflicts children, young soldiers, and new-comers, as, for that matter, does typhoid fever. This immunity is highly effectual, for out of 1000 individuals who had previously suffered from bacillary dysentery, only 3 or 4 were susceptible of contracting it again (Shiga), even when the previous attack had been extremely benign. This explains why an epidemic rarely attacks the same

population two years in succession. The usual interval between the great epidemics of bacillary dysentery is ten to twenty years in the same locality. During this interval there has been time for a fresh generation of receptive subjects to spring up.

The army, on the other hand, offers a continuous receptivity, because it constitutes a collectivity which in time of peace is renewed every two or three years; to it every soldier who has recently joined the ranks brings fresh aliment for an infection against which he has not been rendered immune.

The Determining Causes of Bacillary Dysentery

The bacillus of dysentery may show itself in healthy organisms, unaffected by fatigue, or by conditions of diet, or other factors. The different circumstances already enumerated are, therefore, in reality, only accessories of the infecting germ, which is the sole determining cause of the malady.

Having found its way into the alimentary canal, the bacillus proceeds to localise itself by election in the mucous membrane of the large intestine, and also in a portion of the small intestine, where it provokes the lesions which are special to the malady. The subcutaneous or intravenous inoculation of the bacillus into rabbits, dogs, and cats, etc., results in symptoms and lesions identical with those observed in man.

The dysentery bacillus *lives exclusively in the intestine* of the patient.[1] It is not found elsewhere (if we except the bile). It exists in the stools in considerable quantities. The stools, therefore, are the *essential and exclusive element of dysenteric contagion.*

The most usual mode of contagion is by way of the mouth. Strong and Musgrave caused an Indian condemned to death to swallow a solution of bicarbonate of soda, and then a culture of bacilli two days' old.

[1] Rosenthal, however, has isolated the bacillus from the blood of the heart at autopsy.

After thirty-six hours diarrhœal and mucous evacuations appeared, streaked with blood; their expulsion was very frequent (as many as 31 stools in twenty-four hours), and there was meteorism, with abdominal pains.

Cases of accidental infection by the absorption of cultures (Flexner) have been reported. Dodge has recorded the case of a laboratory assistant who, at the end of twenty-four hours, was attacked by an acute dysentery, a small quantity of a culture having flown into his eyes while he was handling a broken tube.

It is easy to understand that the frequency of evacuations, and the abundance at all stages, and especially at the outset, of the dysentery bacillus in these evacuations, greatly favour the spread of the contagion by the dysentery patient.

This is why *direct* contagion is very common. Hence epidemics in the family, the household, or the village may follow the arrival of a single sufferer. The epidemic spreads like a spot of oil, successively reaching those about the patient, his relatives, the servants, and the neighbours. In country districts especially contagion is easily effected, as the inhabitants, being ignorant of the elementary principles of hygiene, unconsciously expose themselves to the danger of contagion.

Transmission is effected directly by the hands (from the hand of the patient to the hand of the receptive subject), the hands being contaminated by the dejecta, through handling bedroom utensils or slop-pails, body-linen, sheets, etc. From this moment many circumstances may enable the bacillus to obtain access to the mouth of the healthy subject.

In hospitals direct contagion often results in attacks on nurses and students who attend upon dysentery patients, and also on adjacent inmates.

Inter-human contagion operates in the same way in camps, during manœuvres, and, lastly, in time of war, and the transport of the germ is due to the same

mechanism, *more particularly to dirty hands.* The appearance of dysentery in a cook, or a canteen-keeper, or his assistants, is genuinely dangerous in this respect, as direct contagion is then augmented by other modes of contagion, through a great variety of intermediate agencies.

Hence it is that the dysentery bacillus is so readily disseminated by the dejecta of patients, by dead bodies, and by anything that has become contaminated—water, the soil, etc.

The dog, being susceptible to bacillary dysentery, is also able to communicate the disease to man.

Bacillary dysentery is, therefore, one of the most contagious of diseases.

Whatever may be the mode of contagion, whether direct or indirect, the point of departure of the bacillus is always to be found in the fæcal matter of the patient or the carrier. The dysenteric patient is contagious from the onset of the disease, from the appearance of the very first symptoms, although these may appear harmless: such, for example, as diarrhœa.

The period of incubation in bacillary dysentery is on an average from two to five days, sometimes a week. The bacilli are particularly numerous in the stools during the initial period.

The disease is contagious during the whole of its course, and it very commonly remains contagious during convalescence also. There are many examples to prove the rôle of the convalescent in spreading the germ. Moreover, relapses are sometimes observed several weeks after recovery (Shiga). In such cases, therefore, the bacillus had not disappeared. In 1900 a French soldier, convalescent from bacillary dysentery, was the cause, at Vallorbe, by direct or indirect contagion, of twelve cases, with four deaths. Bacteriological tests enable one to find bacilli in the stools after the patients have recovered from the disease.

Thus there are carriers of bacillary dysentery, capable of disseminating the dysentery bacillus with their

excreta, just as there are carriers of typhoid and para-typhoid fever.

Bacteriological researches show that in some subjects the persistence of the bacillus may continue for three or four weeks, for a few months, or even for a year or more. The proportion of these carriers of germs, temporary or otherwise, is 5 to 7 per cent.

It should be noted that with certain of these carriers the persistence of the bacillus is at the same time betrayed by a chronic diarrhœa of a dysenteric nature (H. Vincent), which may continue for one or two years. These subjects are extremely active propagators of the virus. It is therefore important to pay attention to these refractory diarrhœas, which do not always commence with the clinical signs of dysentery, with its mucous and blood-stained dejecta.

The existence of germ-carriers who have never presented (or do not appear to have presented) symptoms of dysentery, or even of diarrhœa (Duval, Jehle, and Charleton), has been verified. These carriers have accordingly to be ferreted out, and it will readily be understood how dangerous they are when they follow callings which entail the handling of food, such as those of cook, butcher, milkman, pastrycook, waiter, etc.

Children are frequently disseminators of dysentery.

The prolonged persistence of the dysentery bacillus in certain subjects, sick or healthy, explains the maintenance of the endemic condition in certain countries, and the appearance of unexplained cases in a village, a house, or a family. Carriers of germs, moreover, suffer from time to time from attacks of diarrhœa, with the passage of abundant stools, which maintain the contagion.

There are, therefore, great epidemiological analogies between dysentery and typhoid fever, the para-typhoid fevers, and cholera.

The bacillus occurs in the gall-bladder of some individuals, but not in all (H. Vincent). If an active culture of Flexner's bacillus is injected into the

veins of a rabbit, or under the skin, or into the peritoneum of the guinea-pig, the bacillus is not always found in the gall-bladder, even when the animal presents the characteristic lesions in the intestine. If the animal is killed at various stages (from eighteen hours to ten days) the bacilli may be found in the gall-bladder (on one occasion it was found after twenty-eight hours), but this is very exceptional. The urine never shows it, but it may be isolated from the spleen and the liver. As a rule it is found in the bile only when the bacilli have been injected into the peritoneum.

In man it has been isolated from the mensenteric glands (H. Vincent).

Amako, having made a bacteriological examination of the bile and the splenic secretion of sixteen individuals who had died of dysentery, was unable to isolate the bacillus.

Further, if the bacillus of Shiga or Flexner is cultivated, in sterilised bile, human or animal, this medium is highly unfavourable. The bacillus does not propagate itself, but generally dies out after a few days (H. Vincent).

Although the bacillus has sometimes been isolated from the human gall-bladder at autopsies, there are certain unknown details which have yet to be cleared up. Does the bacillus form colonies exclusively in the gall-bladder, and if so, under what circumstances ? May it not remain and subsist in the intestinal glands, these becoming the point of departure in the attacks of diarrhœa of which we have spoken ?

Indirect Contagion

To the modes of propagation by contact must be added those by indirect transmission, which also plays an important part in the dissemination of the disease.

Transmission by all kinds of intermediate agents is feasible because the dysentery bacillus is able to

survive outside the human organism for a varying length of time.

Eliminated with the fæces, the bacillus finds its way into the soil, into latrines, into water-supplies, and contaminates linen, food, etc. It is often transported by the patient himself, who, if he is suffering from a benign form of the disease, moves from place to place disseminating the germ. The most recent cases are the most dangerous, especially in compact bodies, such as regiments, schools, factories, etc. It is the earliest stage which corresponds with the most profuse elimination of the bacilli in the stools. When the disease has continued for some days, the bacilli become rarer.

Disseminated in an external medium, the bacilli are not immediately destroyed. Their vitality varies considerably. The bacilli of Flexner's type seem best adapted to survival outside the human body. Those of Shiga's type are far more delicate and frail.

In general, the dysentery bacillus survives longer and more readily in cool and damp surroundings. This is exemplified in the following data.

Vitality of dysentery bacilli :

Damp earth, sterilised	13 to 34 days
Dry earth	6 ,, 15 ,,
Garden soil (surface)	6 ,, 15 ,,
Garden soil at a depth of 12 inches	34 ,, 49 ,,
Soil from a heath	20 ,, 31 ,,
Dry sand (surface)	3 ,, 4 ,,
Damp sand at a depth of 12 inches	29 ,, 39 ,,
Dried cultures	5 ,, 7 ,,
Cultures in bouillon	20 ,, 25 ,,
Cultures on agar	25 ,, 30 ,,
Dejecta buried in the soil	30 ,, 90 ,,
Dejecta on linen (folded up)	more than 30 ,,

Similar investigations have been made in respect to water, exposed to the action of light or in darkness, and under conditions of greater or less contamination.

A culture of Shiga's bacillus was emulsified in water drawn from the River Vanne and sterilised. A

successive series of cultures gave the following results (H. Vincent):—

At the outset . . .	94,000 bacilli per cc.
After 8 hours . . .	77,000 ,, ,,
,, 24 ,, . . .	30,000 ,, ,,
,, 31 ,, . . .	29,500 ,, ,,
,, 48 ,, . . .	13,000 ,, ,,
,, 72 ,, . . .	2,000 ,, ,,
,, 4 days . . .	850 ,, ,,
,, 5 ,, . . .	120 ,, ,,
,, 6 ,, . . .	2 to 14 ,, ,,

This shows that the disappearance in water is suddenly accelerated after the second or third day.

In impure water the vitality of the bacillus does not persist nearly so long. In impure sterilised water the bacillus disappears in ten to twelve days at 14° to 16° C., and in thirteen days at 1° to 4° C. In water drawn from the Vanne, which contained 220 germs per cc., the bacillus persisted for nine to eleven days at a temperature of 15° to 18° C. In very impure water it survives only two to five days at 22° to 28° C.

If these experiments are made with samples of water unequally contaminated by saprophytic organisms, and kept at a temperature of from 2° to 4° C., in order to prevent the excessive multiplication of saprophytes, we find that the bacillus lives only two to four days, and that its disappearance *takes place sooner when the water contains a larger number of common bacteria.* These latter are antagonistic to the pathogenic bacillus. The *Staphylococcus pyogenes*, the *Micrococcus prodigiosus*, the *Bacillus coli*, the *Bacillus fluorescens liquefaciens*, the *Proteus vulgaris*, the anærobic microbes living in water, and the germs of putrefaction, are more especially hostile in their action upon the dysentery bacillus. Even the filtrate of these microbes possesses a deterrent action (H. Vincent).

In ice, and in darkness, the bacillus has been found to survive for forty-one to sixty-eight days.

The action of sunlight is very important. The

bacillus behaves differently, accordingly as it exists in a subterranean body of water, sheltered from the rays of the sun, or in the water of a river or a lake, etc., where the rays of the sun can exert their powerful microbicidal action.

In clear water direct sunlight destroys the bacillus in two to two and a half hours. If the emulsion is rich, so that the water is turbid, the bacillus survives for four or five hours.

In the diffused light of the laboratory it dies in eight days, while in darkness it lives for fourteen days.

Cold, humidity, and darkness are therefore important factors of preservation as regards the bacillus of dysentery. Heat, desiccation, and sunlight, together with the vital competition of saprophytes, are, on the contrary, the most effectual natural means of its destruction.

All these facts find their application in the epidemiology of bacillary dysentery; they explain the frequency of the malady, and its persistence in cold climates, the real though limited rôle of water, the preservation of the germ in the soil under certain conditions, etc.

The receptacles of the dysentery bacillus are, as we have said, very numerous. Latrines, privies, etc., often serve as the connecting link between the sick man and the healthy subject, infection occurring through the medium of boots or shoes, which carry the germ into the house, the kitchen, and the dining-room or mess-room, where it lies on the floor. Finally, the hands may pick up the bacillus.

In armies, in time of peace, and above all in time of war, the cesspits are too often rendered unapproachable by sloughs of filth in which mud and fæcal matter are mingled, and which serve as reservoirs for the germs. After such a microbic foot-bath a man carries the bacillus with him wherever he goes.

Hence we understand why a first case of dysentery may be followed swiftly by an epidemic outbreak, and there are many examples of regiments which have

occupied barracks, camps, or cantonments previously inhabited by men afflicted with dysentery, which have in their turn contracted epidemics, sometimes of a formidable nature.

The *soil* has the power of preserving the bacillus intact, especially in winter and during the rainy season. In 1890 some troops proceeded to install themselves in the camp of Chalons, and dug the emplacements for their tents in ground where old cesspits full of fæcal matter were uncovered. Dysentery had prevailed there the year before. These men contracted dysentery; the rest of the troops were unaffected. Does this explain why, almost every year, at a given date, we see dysentery reappearing with disheartening persistence in certain garrisons—such as Vincennes and Versailles—and in certain camps—such as Chalons? As we shall see farther on, flies also play a part in this periodic return of epidemics.

In country districts the contamination of the soil may contribute in the same way, in addition to direct contagion, to the maintenance of epidemic or endemic dysentery.

It seems established that, notwithstanding the rather limited vitality of the dried bacillus, the admixture of the bacillus with *dust* is capable of propagating dysentery by inhalation. In 1894 a battery of artillery was sent to occupy the camp of Hussein-Dey, near Algiers. In the preceding year there had been an epidemic of dysentery in this camp. After a very violent gale, which raised whirlwinds of dust and sand, and which lasted a week, the men complained that everything they ate and drank was full of earth and sand. A very serious epidemic followed, affecting 15 per cent. of their effectives. Their drinking-water, vegetables, and other rations were wholesome.

During the war in the Transvaal the English physicians attributed the epidemic state of dysentery not to the water, but to dried fæcal matter, and the sandstorms occurring on the veldt. There is no need

to demonstrate the danger of spreading fæcal matter on the soil, and of allowing vegetable crops or surface waters to become contaminated with it. The cultivation of vegetables in market gardens by means of this barbarous method of manuring exposes large numbers of persons to the danger of infection.

Cases of contagion by means of clothing worn by patients, their underclothing, sheets, shirts, etc., have been reported. The washerwoman's calling exposes her in a special manner to contagion.

In camps and cantonments soiled bedding-straw may be a factor of contamination.

Contaminated food-stuffs also play a by no means negligible part in the transmission of the disease, whether they have been handled by persons suffering from acute or chronic dysentery, or have been in contact with soil impregnated with fæcal matter (as may be the case with vegetables and fallen fruits), or have had the germs deposited upon them by flies.

The contamination effected by persons suffering from dysentery, or by carriers of the germ, is usually due to unclean hands, the patient or carrier having neglected to wash them after visiting the closet or privy. The bacillus survives for thirty days on bread, rice, cooked meat, etc.

In addition to direct contagion, it is an undoubted fact that flies (*Musca domestica*, *Calliphora vomitoria*, *Lucilia cæsar*), which carry a large number of infectious agents, *play a very important part in the propagation of bacillary dysentery.* In temperate countries it is at the time of their pullulation—that is, during the hot season—that the epidemic curve reaches its maximum. Further, it is easy to realise how great must be the influence of flies when one considers their innumerable flights, from fæcal matter, where they gather the bacilli with trunk and legs, to food-stuffs of every kind—meat, vegetables, bread, milk, pastry, cheese, sweets, etc., which they may also infect with their excrement. If we feed flies (*M. domestica*) under

a sterilised bell-glass on a culture of dysentery bacilli the bacilli may be found in their excreta for four days afterwards. Many of the flies succumb (H. Vincent).

Propagating agents of great mobility, flies bring the pathogenic bacilli from the open air and introduce them into dwelling-houses, into kitchens and dining-rooms, and even deposit them on the skin of the face, especially in the case of young children. They have justly been blamed for the epidemics observed in the Indies, and also during the Spanish-American War, the Boer War, the Manchurian Campaign (Kolosky), and the present war, in which their extraordinary frequency, during the hot season, has been observed.

They may also infect milk. The contamination of milk may further be effected by farm servants afflicted with dysentery (Finny), by carriers of the germ, by its mixture with impure water, or by the employment of receptacles which are unclean and specifically contaminated.

It goes without saying that it is only the drinking of unboiled milk which is dangerous, as boiling instantly destroys the bacillus. Even dried milk, cream cheese, butter, and cheese may serve as receptacles for bacilli deposited by flies or by human hands, and will preserve them alive for some days.

It was formerly believed that *drinking-water* was most commonly concerned in the propagation of epidemic dysentery. This, however, does not appear to be the case—at all events, where the dysentery bacillus is concerned. It is undeniably a fact that the bacillus may be introduced into the organism by means of drinking-water, but it is not so frequently introduced in this way as is the bacillus of typhoid. Shiga has recorded a village epidemic due to water, in which 413 cases were observed. On the other hand, however, a large number of bacteriological analyses of water, made at the very outset of various epidemics of dysentery in the Val-de-Grace laboratory, as well as in local laboratories, have

only as an exception revealed the pollution of drinking-water.

During the epidemics observed in the camp of Hussein-Dey, in 1894 and the following years, the water, furnished by an artesian well, was extremely pure. On the occasion of the malignant epidemics which occurred in the garrison of Versailles the water, which was bacteriologically examined on the appearance of the first cases, was irreproachable in quality. The short period of incubation obtaining in dysentery confirms the complete validity of these examinations.

Similarly Faichnie has reported the occurrence of epidemics in the British Army, although the men were drinking only boiled water and tea.

It may be concluded, then, that drinking-water may cause an outbreak of dysentery, but that it is by no means the most important propagating agent of this disease.

An explanation of this fact is that water is not a favourable medium for the preservation of the Shiga-Flexner bacillus, while it is even less favourable to its vegetation. In water contaminated by numerous germs, as are those waters to which the dysenteric bacillus makes its way, together with all the rest of the bacilli found in fæcal matter, and the germs of putrefaction, the bacillus can hardly live longer than two or three days. It quickly becomes rare, and then disappears. The saprophytic microbes, ærobic or anærobic, exert a vigorous competitive action, and are inimical to its survival, especially when the temperature of the water is fairly high, and therefore favourable to their multiplication.

Flexner's bacillus is a little more resistant in water than is Shiga's bacillus. Both are very sensitive to light.

Water becomes polluted in a great variety of ways. These are the same as those described in connection with the etiology of typhoid fever, the paratyphoid fevers, and cholera: the direct discharge of fæcal

matter in sewage; the action of rain, which washes the soil and bears impurities along with it; infiltration into the subsoil; contamination due to neighbouring cesspools; the use of fæcal matter as manure; the washing of the linen of dysentery patients or carriers, etc.

In cesspools the antagonistic influence of saprophytic bacteria considerably diminishes the vitality of the dysentery germ.

Climatic conditions may mitigate this automatic process of purification in the water, the soil and the subsoil. Cold, while it prevents the development of saprophytes, actually helps to preserve the bacillus of dysentery.

This is an interesting fact, and worthy of record, for it partly explains the persistence of dysentery in northern countries.

In lake waters, where the light is able to act on the germs (the luminous rays penetrating to a maximum depth of five metres), the superficial strata may be purified, but the deeper levels may remain contagious. The same conditions obtain in the waters of the Durance and the Rhone.

The Spread of Epidemics

Bacillary dysentery may exist endemically, giving rise to isolated cases, but it more often occurs in epidemics. Then, especially in new countries, it gives rise to numerous cases, occurring rapidly and over a wide area, attacking a large number of victims simultaneously. Amongst large collections of people, for example in barracks and schools, where human contact is frequent, the spread of epidemics is often alarming. Every day fresh cases appear—of apparently simple diarrhœa, or of typical dysentery. The epidemic lasts a few days or weeks, and ceases, either because the receptive soil has become exhausted, or because effective prophylactic measures have been taken.

In country districts, where the rules of hygiene are ignored, where dejecta are scattered everywhere, and where children maintain the epidemic state by contracting attenuated or unrecognised forms of the disease, dysentery is sometimes more tenacious, and may continue for several months. In such epidemics the mortality is high.

This is the case in Japan, where dysentery has been prevalent for centuries, often with disastrous effects. Between 1892 and 1896 it caused 50,000 deaths (Shiga). Between 1890 and 1900 there were 875,534 cases, with 26·39 per cent. of deaths.

When dysentery breaks out in a small village it is not long before it attacks all the receptive subjects (5 to 10 per cent. of the inhabitants in Japan). In the following year there are few cases or none. If the first appearance of the epidemic has been slight or moderate, a more violent return is often observed in the following year. In the third year no cases occur, the inhabitants having become immunised.

In towns dysentery attacks more especially the populous quarters and poor families, in which parents and children live in close mutual contact; here there are the greatest facilities for contaminating one another.

CHAPTER VI

EPIDEMIOLOGY OF AMŒBIC DYSENTERY

The existence of pathogenic protozoa in the intestines of a dysentery patient was proved by Lösch, who succeeded in reproducing the disease in the dog, by causing the latter to absorb dysenteric dejecta.

The parasites (*Amœba coli*, Lösch) reproduce themselves by division and by the formation of cysts, which give rise to several daughter amœbulæ.[1]

Various apparent species of the dysenteric amœba have been described: *Entamœba histolytica*,[2] *E. tetragena*, *E. tropicalis*, *E. nipponica*, etc. The first is the most frequent. They are very often accompanied by other parasites: *Trichomonas intestinalis*, *Lamblia*, etc. (Simonin).[3]

As has been said, amœbic dysentery is more especially the appanage of hot and tropical countries. Very common in India, Cochin-China, Tonkin, Sumatra, Java, Madagascar, the Sudan, Central Africa, Egypt, Senegal, etc., it is equally prevalent in South America, Brazil, Cuba, and the Philippines. Tonkin, and above all Saigon, is, for the French troops, a dangerous centre of amœbic dysentery. It is not rare in Morocco.

The admirable work of Osler, and of Councilmann and Lafleur, and the important investigations of Gasser in

[1] *A. coli dysenteriæ* is a more explicit denomination, as is *Entamœba dysenteriæ*. The latter was proposed by Councilmann and Lafleur. [*A. coli dysenteriæ*, according to the rules of nomenclature, is not a permissible name, however suitable it may be as a descriptive term.—Ed.]

[2] *Entamœba histolytica* is the name employed in England at present for the pathogenic amœba.—Ed.

[3] A new non-pathogenic amœba has recently been described by Wenyon and O'Connor and by Dobell and Miss Jepps. It has been called *Entamœba nana*—Ed.

Algeria, of Marchoux in Senegal, and of Harris, etc., have helped to throw light upon the nature and the modes of transmission of this form of dysentery.

For a long time it was supposed that amœbic dysentery could not exist in cold or temperate countries, save as a very exceptional malady, or one affecting subjects infected in the colonies or other hot countries. The discovery of the *Entamœba* in a certain number of cases occurring in Russia, at Kiev (Massioutine, Kourlov), in Prague (H. Lava), in France (Landouzy and Debré, Caussade and Joltrain), and in Spain (Fidel Fernandez Martinez), as well as the more recent discoveries made during the present war, in the case of European soldiers infected in the trenches (Ravaut and Krolunitsky, Job, Richet, jun., Rist, Rathéry, etc.), has demonstrated the fact that this disease should be looked for, and is perhaps more common than is supposed, in temperate climates. Amœbæ have also been found in cases of suppurative hepatitis in Russia, Austria, Paris (Caussade and Joltrain), etc.

Having made their way into the alimentary canal [as cysts], the young amœbulæ localise themselves in the mucous lining of the large intestine. This is their seat of election. They may also be found in the vermiform appendix, where they may give rise to appendicitis (Harris); further, they frequently occur in the hepatic parenchyma, where, transported by the veins, they form colonies, giving rise to actual local necrosis, the hepatic abscess. Localisations in the lungs, spleen, brain, and articulations are more unusual.

In the intestine the amœbæ find their way into the Lieberkühn follicles, and then—after the destruction of their walls—into the glandular interspaces, the submucous tissue, the lymphatic spaces, the capillary blood-vessels, etc.

The infection may be conveyed by inoculation to the dog and the cat, and the progress of the parasite may then be followed through the elements of the intestinal walls.

The discovery of amœbæ in abscesses of the liver,

and, above all, in their walls (Rogers), has finally established the relations which Kelsch had stated to exist (basing his statement on clinical observation and pathological anatomy) between dysentery and hepatitis.

The multiplication of amœbæ in the walls of the large intestine results in the anatomical destruction of the tissues and the formation of extensive ulcerations of the colon. This destruction is facilitated by additional microbic infections.

The point of departure of the amœbic contagion is therefore to be found, as in bacillary dysentery, in the intestine of the patient, and, practically, in his dejecta. The latter sometimes contain an enormous number of parasites (amœbæ or cysts), especially in recent and acute cases. They are, however, also numerous in the chronic forms, and come from the intestinal ulcerations and their secretions.

It should be added that when dysenteric abscesses of the liver have found an external opening, usually through the right lung and a bronchial fistula, the parasites exist in the vomicæ, and may, though the case is rather exceptional, be transmissible by this secretion.[1]

Unlike bacillary dysentery, which almost always follows an acute development, amœbic dysentery habitually becomes chronic when the treatment opposed to it is insufficient. Bacillary dysentery immunises the infected subject; amœbic dysentery does not. It follows from this that in patients suffering from chronic amœbic dysentery the excretion of the parasites is a very long process. But this is not all. In soldiers recalled from Tonkin, etc., and returning to France, the fæces may, after (apparent) recovery, still contain *A. coli dysenteriæ* [*E. histolytica*] or its cysts. Sometimes these patients have, or appear to have, entirely recovered; sometimes, at irregular intervals, they suffer from attacks of diarrhœa. They are true *carriers* of amœbæ or their cysts. There are even some

[1] If this were so it would mean that cysts were formed in these situations. There is no proof so far of such an occurrence.—Ed.

who suffer from a return of dysentery after a remission of six or eight months, or even a year (H. Vincent).[1] These carriers are propagating agents of the dysentery amœba, through the medium of their excreta. Cysts may be found in *healthy subjects* dwelling in infected countries (Mathis, Ravaut and Krolunitsky).

It is easy to understand how amœbic contagion is effected among soldiers fighting at the front or living in cantonments. This is the explanation of the fact that cases occur among soldiers who have never been in the colonies.

In times of peace, moreover, numerous examples of amœbic contagion have been observed on board vessels returning to France with convalescents, healthy subjects, and dysentery patients simultaneously. In a barracks occupied by colonial troops, at Toulon, some soldiers living in contact with comrades who had returned from the colonies contracted amœbic dysentery (H. Vincent).

As the pathogenic agent of amœbic dysentery resides exclusively in the fæces, it is accordingly susceptible of being directly transmitted by the latter.

Immediate contagion, therefore, is the propagating agent of the amœba. Instances have been published of contagion in hospital orderlies or persons living in contact with patients suffering from amœbic dysentery (Dopter, H. Vincent, Lemoine). Again, the patient may contaminate those surrounding him by touching articles of food with unclean hands. On the other hand, the absence of precaution on the part of those who are tending the dysentery patient may transfer the germ in the same way.

Experimentally, if young kittens, infected by the rectum, are placed in a cage together with other healthy ones, the latter may acquire dysentery by contagion. Female cats, suckling their infected young and licking them, will contract dysentery. A post-mortem examination reveals innumerable amœbæ in the large intestine.

[1] Low has recently described a case of liver abscess occurring twenty years after the original attack of dysentery.—Ed.

They are sometimes found in the small intestine as well.

The *indirect* transmission of *A. coli dysenteriæ* [*E. histolytica*] is rendered possible by the fact that the parasite, although rather lacking in vitality, is yet able to survive by living in the encysted state, thereby resisting the natural causes of destruction.

In the ordinary state, not encysted, it is killed in thirty-five minutes at 45° C. (Marchoux) by gastric juice, acids, antiseptics, etc. Urine, even when neutralised, destroys amœbæ (Harris). Boric acid does not appear to have any appreciable effect, but osmic acid and sublimate instantaneously arrest the amœboid movements. Experiments made with recent stools of dysentery patients have given the following further results :—Solutions of permanganate of potash act feebly on Entamœbæ ; solutions of tartaric acid, citric acid, oxalic acid, and more particularly of tannin, and oxygenated water, kill them rapidly (Harris). Neutral hydrochlorate of quinine [Quinine bihydrochloride], even in very minute quantities, in a solution of 0·50 gr. to 1 c.c. of water, placed at the edge of the cover-glass, has an overwhelming effect. The amœbæ become instantly retracted, forming unrecognisable masses. They are quickly killed by Labarraque's solution (5 or 10 per 1000), less quickly (in one to five minutes) by a solution of methylene blue or by neutral red (H. Vincent).

The amœba of dysentery, however, resists desiccation, thanks to its property of forming cysts. It is not always destroyed by freezing (Künen and Swellengrebel). If kittens are made to swallow fresh dysenteric dejecta they do not contract the disease, but if the dejecta are allowed to dry the parasites have time to become encysted, and the animals acquire the disease. The cysts resist the gastric juice, but in the small intestine their envelope is dissolved by the alkaline secretion of the latter, and on reaching the large intestine they proceed to multiply.

This explains why the dysentery amœba is able with impunity to traverse the stomach, despite the presence of the gastric secretion, to which it is susceptible, as to all acids.

Its transmission by means of food-stuffs, fruits, vegetables, etc., contaminated by the spreading of manure, is therefore possible. Flies are probably capable of transporting it by means of their legs or their dejecta, and there is room for further investigation in this direction.[1]

It has sometimes been suggested that contagion may be effected by means of the seats of closets, or rectal catheters or thermometers which have not been disinfected.

Another fact of great importance is that the pathogenic amœba, above all in the encysted state, is capable of survival for at least nine to thirteen days in water, such as well-water, ditch-water, or the water of ponds, where it is able to enjoy a certain amount of obscurity. It has not been observed that it multiplies there, but the fact of its survival explains the frequent transmission of dysentery by means of polluted water. It is possible that the amœba is able to multiply in muddy places, for when in the human intestine it is able to feed on bacteria as well as on the corpuscles of the blood.[2] The dysentery amœba is, therefore, enabled to resist a certain number of natural causes of destruction owing to its property of becoming encysted.

One of the best established and most frequent modes of propagation of the amœba results from the absorption of polluted water. It has been noted that this parasite subsists in water. Long ago Léon Colin in Algeria, H. Blanc in Abyssinia, Lalluyaux d'Ormay in Cochin-China and Barailler in Guadeloupe called atten-

[1] *Vide* Wenyon and O'Connor's recent experiments, and the work of J. G. & D. Thomson in Egypt.—Ed.

[2] There is no evidence of this. The living amœbæ quickly die when they leave the body. So far they have never been cultivated. It is by the cysts that propagation takes place.—Ed.

tion to the important part played by drinking-water in the etiology of dysentery. In Guadeloupe it was remarked that while the water of the River Dugommier was productive of dysentery, the water of the tanks and cisterns was not. A. Calmette has noted that the epidemic of dysentery which prevailed in the arrondissement of Loctrang, in Cochin-China, disappeared when water filtered by Chamberland filters was provided. In the Dutch Indies the employment of purified water has yielded equally favourable results.

Serious epidemics of dysentery used formerly to be observed on board warships, which were attributed to the drinking of water drawn from the rivers of the Far East, particularly in Saigon and Hong-Kong.

Amœbic dysentery is thus almost always associated with a defective hygiene or a bad food-supply. It is observed among the poor populations of hot countries, and in soldiers suffering from sea-sickness and improperly fed, or who do not observe any precautions.

It is a malady of all seasons, but is nevertheless more common in summer. It is, according to Harris, less frequent in children than in adults.

All the epidemiological data which have just been given apply equally to the suppurative hepatitis of hot countries, which is nothing but a hepatic dysentery. The history of hepatic abscess is, indeed, as closely bound up with that of dysentery as is the history of orchitis with that of mumps. The geographical distribution of the two diseases is the same,[1] and the frequency, or even the mere existence of hepatic abscess in a district enables one to affirm the presence of amœbic dysentery. This is why suppurative hepatitis, so often observed in hot or tropical countries, is very exceptional in cold or temperate countries, where bacillary dysentery is, on the contrary, predominant, if not exclusive.

Even before the discovery of Entamœbæ in the walls of the abscess (Dock, Osler, etc.), the specific nature of

[1] Though this is so, some parts of the tropics show many more cases of liver abscess than others. India for example.—Ed.

the latter had been affirmed by Kelsch, and also by Laveran, Netter, and Peyrot. Marchoux succeeded in causing amœbic abscesses by injecting pus from dysenteric abscesses into the portal vein of a cat.

Amœbic hepatitis is most frequently preceded by a characteristic or ill-defined dysentery. In certain cases, however, the abscess of the liver may precede the dysentery, or may even occur in the absence of any appreciable condition of dysentery. The hepatitis then represents the primary localisation of the amœba, but its initial penetration by way of the intestine, and thence through the portal radicles, does not appear to be in doubt.[1]

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We have yet to speak of *mixed* cases of dysentery —that is, cases where the subject is infected simultaneously by the bacillus of dysentery and the *Entamœba dysenteriæ* [*E. histolytica*]. The first discovery of these dysenteries, which we shall call amœbo-bacillary dysenteries, was made by Strong, in the Philippines and the United States. Having examined 246 cases of dysentery in the Philippines, he found that 193 were amœbic, 50 were bacillary, and 3 were mixed.

While the present war against Germany has enabled us to verify cases of autochthonous amœbic dysentery in France, it has also afforded opportunities of observing cases in which the patient was infected simultaneously with bacillary and amœbic dysentery. In August, 1915, P. Ravaut and Krolunitsky described a mixed epidemic, sometimes attacking men belonging to the colonial or Morocco regiments, and sometimes soldiers of all ages who had never left France, but who had been living in contact with the former, or occupying the same trenches.

Roussel, Brulé, Baral, and A. P. Marie have made bacteriological observations similar to those of the above-mentioned writers.

It is as well to be aware of the existence of these

[1] Autopsies certainly bear this out, signs of ulceration, old or recent, being present in the large intestine.—Ed.

amœbo-bacillary cases, although they are not very common as compared with the individual cases of bacillary or amœbic dysentery.

There are also, for that matter, unconnected with the circumstances of warfare, epidemics in which sometimes the dysentery bacillus and sometimes the *Amœba coli dysenteriæ* [*E. histolytica*] are encountered in members of the same group of people. Strong and Musgrave found that out of 1328 cases of dysentery occurring among the American troops under treatment in No. 1 Reserve Hospital, in Manila, in ten months, 561 were of the amœbic type, while 766 were bacillary.

Nevertheless, the fact remains that cases of mixed dysentery may be observed, and this is a point of great interest from the epidemiological and prophylactic as well as from the therapeutical point of view.

. . . . . .

There are other affections which enter into the dysenteric syndrome, but which, by reason of their rarity, have not the great importance of the diseases already discussed.

In their writings on dysentery Councilmann and Lafleur were the first to express the opinion that dysentery is not a single disease, but " that there are dysenteries just as there are broncho-pneumonias." Although very greatly predominant, bacillary dysentery and amœbic dysentery are not, properly speaking, the only forms of dysentery. *Balantidium coli* (Strong and Musgrave), *Chilodon dentatus* (Guiart), *Schistosoma mansoni*, a special spirillum (Le Dantec), and kala-azar parasites (Leishman-Donovan bodies), etc., may give rise to an acute or chronic colitis, which is closely analogous to the classical form of dysentery.

The truth is that the living organism cannot oppose infecting germs by an unlimited number of reactions.

Balantidium coli exists in great profusion in the ulcerations and the walls of the large intestine of the sufferer, as well as in his evacuations. Its vitality outside the living organism is increased by its power

of becoming encysted. The cysts (80μ to 100μ in diameter) are formed more particularly under the influence of desiccation. This ciliate, when not in the encysted state, is very fragile, and sensitive to acids (even when diluted to a strength of 1 in 1000), to quinine (1 in 1500) (Klimenko), etc. It may live for three days in water.

Common enough in the pig, *Balantidium coli* is probably transmitted by the latter, or else by the dejecta of patients suffering from this form of dysentery; but only when the parasite has assumed the encysted form, which protects it against the action of the gastric juice. The Balantidian form of dysentery is observed more particularly among pork butchers.

Attempts at experimental inoculation of animals have, however, failed (Manson), and such experiments have also failed even with human subjects, despite the existence of cystic bodies (Grassi and Calandruccio).

The existence of *Chilodon dentatus* has been noted by Guiart in the dejecta of a patient exhibiting a dysenteric syndrome.[1] Billet considers that *Trichomonas intestinalis* may also produce an analogous disease. He has observed four cases of this kind. Bilharziasis, according to Manson, is transmitted by the embryo of the Schistosoma, which, having reached the water, finds its way into the body of a fresh-water animal, and through the medium of the latter enters the human host. Drinking-water is thus the infecting agent in Bilharziasis.[2]

[1] As already pointed out, vide page309 *Chilodon dentatus* is a free living protozoon and not parasitic. It can be found in ordinary water taps. Its occurrence in Guiart's case must then have been purely accidental, from some water contamination.—Ed.

[2] Leiper has recently demonstrated in Egypt that the bilharzial miracidium passes into a mollusc. After having developed in the tissues of the snail, cercaria appear and escape into the water. From there they pass directly through the skin of the human host, and so bring about the infection. Wading or bathing in infected water is very dangerous, and will speedily result in the acquisition of the disease. Schistosoma japonicum infections are brought about in the same way.—Ed.

CHAPTER VII

PROPHYLAXIS OF BACILLARY AND AMŒBIC DYSENTERIES

Bacillary dysentery and amœbic dysentery present a large number of common etiological factors.

The prophylaxis of the two diseases accordingly comprises rules which are applicable to either. All disorders of intestinal determination may, from this point of view, be classed together, and the prophylactic measures recommended in the case of cholera will equally apply here.

Among the measures which bear upon the favouring causes, the medical officers of the navy and colonial physicians especially recommend the avoidance of chills in the abdomen in those countries where dysentery is prevalent. One should certainly not disdain the influence of " secondary " causes, and supervision should be exercised over the diet, which in times of epidemic ought to be wholesome and simple and free from indigestible material.

The abuse of biscuits, and preserved meats, and the absence of fresh food have been incriminated, in time of war (the Crimean and Balkan wars), as factors which irritate the mucous membranes of the digestive tract and cause indigestion. The diarrhœa known as " trench diarrhœa " may, as a matter of fact, be due to various germs : enterococcus, *Proteus vulgaris*, etc., as well as the dysentery bacillus.

The general cleanliness of dwelling-houses, barracks, privies, latrines, etc., and their surroundings, is evidently a condition favourable to proper hygiene. In working-class dwellings and poor quarters it should

be seen that this condition is fulfilled, as well as that of individual cleanliness, and it is important to combat alcoholism and take measures to prevent physiological want and over-exertion, which are predisposing factors of infectious diseases.

Microbic or parasitic *prophylaxis* ought to include the compulsory notification of cases of bacillary or amœbic dysentery, owing to the gravity of these diseases, the frequency of epidemics, and the excessively contagious nature of the germ.

This is why the isolation of patients attacked by bacillary dysentery must at once be effected. The evolution of this malady is generally brief (although chronic forms exist), which may facilitate this measure.

Further, it is necessary to take precautions in respect to convalescents and subjects who are or may become carriers of the germ. Consequently recourse to the *laboratory* is an indispensable part of the rational prophylaxis of dysentery. In the army these laboratories, which in time of peace already existed in each regional division, have rendered great service in the early diagnosis of infectious diseases and in hunting out carriers of bacilli. Similarly, in time of war the laboratory of the army corps or army should be consulted as to the exact diagnosis of dysenteries.

Whatever the pathogenic agent may be, the dejecta are certainly the medium of its propagation. It is therefore necessary to disinfect them as soon as emitted, by means of creosol, lysol, or a 5 per cent. solution of copper sulphate, a little hydrochloric acid being added to this last if needful. Sulphate of iron is not an efficient antiseptic.

Latrines, cesspits, and their approaches, in camps in time of war, should be generously sprinkled with chloride of lime, once a day in winter, twice a day in summer. The installation of the water-carriage system of drainage in barracks is a measure of the greatest utility.

Laboratory examinations should be made, not only in

those cases of dysentery which are characteristic in their clinical aspect, but also in ill-defined or attenuated forms of the disease, in cases of benign diarrhœa, and in the sporadic cases which are the forerunners of an epidemic and which are very often due to the specific agent of the disease. During the course of the epidemic these merely diarrhœal forms are no less contagious. It is therefore necessary to take the same precautions as to isolation and disinfection where these are concerned, and to give the patients due attention.

Everything that may have been contaminated by the dejecta is dangerous. It is therefore as well to warn the patients themselves of their contagious condition.

The bacteriological analysis of drinking-water should be made immediately upon the appearance of cases of dysentery, whether in town or in country, or in houses where wells are the source of supply. The same measure is obviously to be applied to soldiers, who must be forbidden to visit taverns and public-houses where non-purified water is served.

It must be remembered that amœbic dysentery in particular is very frequently due to the employment of contaminated water or food. Water should, therefore, before use, be sterilised by boiling or filtration, and vegetables and fruits should be cooked.

All the prophylactic measures which have just been mentioned are of particular importance in time of war, when the incessant contamination of the soil, sub-soil, and water supplies, the frequent presence of germ-carriers, and the inactivity obtaining in cantonments, and, above all, in the trenches, result in exposing the soldier to constant contagion. The prophylactic measures taken should accordingly be particularly stringent, for the dysentery which visits armies in the field is often of alarming gravity. The medical officer should pay special attention to the cleanliness of latrines, etc., their rigorous and repeated disinfection,

the elimination of dung-hills, the scavenging of roads and water-courses, the filling in of depressions in the soil and the systematic destruction of flies, those disastrous carriers of disease germs.

As regards human germ-carriers, we know that the carriers of dysentery bacilli do not retain these microbes very long. Such individuals should be isolated and subjected to intestinal disinfection. Those who are chronic carriers of amœbæ may efficaciously be treated by a daily enema of Labarraque's solution (8 or 10 per 1000), preceded by an ordinary enema to produce evacuation (Vincent).[1]

Military patients are often dilatory in presenting themselves for examination, fearing to be placed on diet, or hoping to avoid being sent to hospital. In this way the pathogenic bacillus very quickly spreads through the barracks, cantonments, camps, or trenches. It is therefore necessary, directly the first cases make their appearance, to request the men, by means of notices and by word of mouth, to consult the medical officer immediately any suspicious symptoms appear.

The clothing belonging to dysentery patients, and carriers of germs, especially their underclothes (vest, shirt, and pants), with trousers, sheets, etc., should at once be sent to the oven for disinfection.

Healthy subjects, and those who are tending the sick, as well as carriers of germs, should wash their hands frequently, especially when they have to handle articles of food.

The careful washing of the hands before meals should be recommended, in order to prevent the propagation or ingestion of the dysentery bacillus or amœba. As regards the amœba, the hands must be washed if they are soiled with earth, mud, filth of any sort, or vegetable

[1] The antiseptic enema should be administered warm (98·4° F.), drop by drop, very slowly, the subject lying in the right-hand dorso-lateral decubitus.

[Such injections probably never reach the cæcum and upper parts of the colon. If the dysenteric ulcers are situated there they can have no effect upon them.—Ed.]

refuse; lastly, and above all, if there has been any contact with a dysenteric patient.

In civil or military hospitals the various measures relating to the sick and their personal effects are easily taken. It is otherwise in the case of poor families and in country districts, the ignorance of the inhabitants in respect of the rules of prophylaxis being absolute. This explains the prompt diffusion of the bacillus of dysentery. Sanitary or medical officers should visit such districts and give practical advice to all the inhabitants.

As regards permanent camps, we cannot too strongly insist that they should be situated on high ground, on a sloping surface, and that all roads, as well as the ground on which the tents or huts are erected, should be made impermeable. Flagged or tarred surfaces will be found extremely serviceable.

If an initial case of dysentery occurs the patient must be immediately isolated. His effects and his bedding must be disinfected; the tent should be struck, the canvas disinfected, and all straw bedding burned on the spot. The patient must never be tended on the spot, but must be sent into hospital.

Dejecta are usually received by the soil (cesspits), or by portable tubs. It would be preferable, in permanent camps in time of peace, to install water-carriage systems of drainage, or to destroy all dejecta by means of heat, in special destructors such as have been proposed for the purpose; but these measures have not yet been adopted.

Consequently, sites must be avoided which have previously been occupied by soldiers suffering from dysentery. It has been recommended (at the camp of Chalons) that infected emplacements should be ploughed up and cultivated.

The latrines and their approaches should be lit at night, and the deposition of dejecta elsewhere than in these places must be strictly prohibited.

Contamination of the soil by the accumulation of

excrement is to be avoided. If cesspits are employed they should be as far as possible from kitchens and mess-rooms or tents, as well as from stables or horse-lines; and they should not be situated in a quarter of the camp from which prevailing winds blow. When the cesspits are filled and their contents covered up after disinfection, their position should be indicated by a sign-post.

Depressions in the soil in the neighbourhood of kitchens, tents, huts, etc., should be filled up with rubble, clinkers, etc. Measures should be taken to prevent the accumulation of stagnant water, kitchen refuse, dung-hills, manure-pits, etc.—in a word, anything that may attract flies and harbour pathogenic germs.

Soldiers suffering from dysentery or diarrhœa, and recognised carriers of dysentery bacilli or amœbæ, must be strictly forbidden to enter the kitchens and must on no account assist in the preparation of food.

Cooks, butchers, pork butchers, pastry-cooks, dairymen, etc., who are suffering from dysentery or are carriers of germs, are active and almost always unrecognised propagators of the disease.

In times of epidemics, or in hot countries where amœbic dysentery is prevalent as an endemic disease, it must be remembered that flies often carry the germ. Accordingly, kitchens, dining-rooms, and mess-rooms, etc., should be provided with screens of wire gauze fitted into the windows and over the doorways; these will exclude the flies. Food must be protected by means of dish-covers or covered with clean napkins.

The destruction of flies may be effected by means of fly papers or catchers (adhesive or poisonous), or fly-traps, or by placing on the tables, at night, plates containing ordinary beer, with the addition of $\frac{1}{5}$th part of formalin. This mixture is a perfect fly-killer.

During epidemics the use of raw vegetables (radishes, salads, etc.), and fruits is to be forbidden, as these may have been contaminated by fæcal matter, either by the

hands of germ-carriers or by flies. In the army the medical officer should supervise the bill of fare of each company.

During the Manchurian War the Japanese derived some advantage from the daily employment of creosote pills as a preventive.

Preventive serotherapy affords protection only for a limited number of days (ten to fifteen at most), and consequently is not a practical measure. It is not to be recommended, especially as regards large bodies of men. It might be employed in families.

Active immunisation by means of cultures derived from dysentery bacilli has not up to the present become a matter of current practice. Shiga made experiments in the vaccination of animals. He mixed dead cultures with an anti-dysenteric serum, and, having sensitised them, injected them into a rabbit; the latter was then able to receive non-sensitised vaccine, and then the living virus.

Having vaccinated himself, Shiga reported a considerable degree of painful œdema at the site of the injection, with fever, severe headache, etc., lasting for several days.

Between 1898 and 1900 he vaccinated 10,000 Japanese by means of dead cultures, first sensitised and then not sensitised. The dose first injected was half a platinum loopful of a culture twenty-four hours old, sown on agar. Four days later he injected twice as much, not sensitised. The injection was made into the cellular tissue of the lumbar region.

The only result of this experiment was the diminution of the death-rate, which, among the vaccinated, fell to 0. But the morbidity was little affected.[1]

Castellani has practised vaccination against bacillary dysentery, mixing anti-dysenteric vaccine with anti-

[1] Animals may be more readily vaccinated against the dysentery bacillus than man. In mice immunity is obtainable in 40 to 50 per cent. of cases; there is first a phase of sensitiveness as regards the virus, and then a phase of immunity, lasting from four to six weeks (Dopter).

cholera or anti-typhoid vaccine. This writer considers that anti-dysenteric vaccine should be prepared with several races of bacilli. Cultures made in bouillon yield an extremely painful and troublesome vaccine. He consequently employs cultures on agar or in peptonised water, sterilised by means of carbolic acid.

J. D. Thomson has investigated the same subject at the Lister Institute. Anti-dysenteric vaccine prepared by heating or sensitising was found to be toxic and painful. Heating does not diminish its toxicity, and, according to Thomson, destroys its property of causing the formation of the specific sensitiser. He prefers vaccine sterilised by carbolic acid.

Dean and Adamson have proposed the preparation of a non-toxic heated vaccine, treating it with equal parts of eusol (1 in 500), and a solution of an alkaline hypochlorite; this eliminates its toxicity by oxidation.

Two injections of the bacilli thus treated are made (100,000,000 at the first injection; then, ten days later, 800,000,000; and a third injection of 200,000,000 of bacilli which have been exposed to heat).

ASIATIC CHOLERA

PART I.—CLINICAL SURVEY

CHAPTER VIII

SYMPTOMATOLOGY

The term *cholera* denotes a syndrome the principal characteristics of which are an extremely abundant gastro-intestinal flux, accompanied by algidity, vomiting, and cramps (Asiatic cholera, Cholera nostras, Stibial cholera, Cholera infantum, Chicken cholera, etc.).

The endemo-epidemic malady whose specific agent is known as the cholera vibrio, or, by reason of its usual form, the "comma bacillus," will alone be considered here.

There is not one single cholera vibrio, but various races of cholera vibrios, which possess characteristics of their own, and these characteristics sometimes present considerable differences.

Their pathogenic action in man is clinically uniform, and gives rise to a series of symptoms which may be divided, schematically, into four periods :

1. The period of incubation.
2. The initial period, or period of invasion.
3. The choleraic period, or attack.
4. The period of reaction.

1. The Period of Incubation. — The Constantinople Conference adopted the opinion that this period does not, in the majority of cases, exceed a few days. In reality its duration is variable. According to Thoinot, it varies between a minimum of a few hours and a maximum of five or six days ; it may, however, exceed this.

2. **The Initial Period, or Period of Invasion.**—Diarrhœa is the dominant symptom of the period of invasion. In temperate countries it is observed in two cases out of three (Guérin); in hot countries it is rarer, the disease often commencing at the first onset with the choleraic period.

This diarrhœa, known as *premonitory* diarrhœa, usually appears at night (Jaccoud).

The stools, fæcal, liquid, green, or the colour of *café au lait*, or sometimes simply serous, possess no particular characteristics. More or less abundant and frequent, they are accompanied neither by straining nor tenesmus. The patient suffers from loss of appetite, flatulence, borborygmi, lassitude and intellectual torpor. The tongue is like that of indigestion, and there is a pronounced thirst. Sometimes certain nervous phenomena are observed (vertigo, severe headache, palpitation, faintness, lassitude, and epigastric pains). These symptoms may persist for a few hours only, or for as long as a week, or more usually they last from twenty-four to seventy-two hours (Thoinot). They then suddenly give way to the choleraic period, or attack.

3. **The Choleraic Period, or Attack.**—The attack usually occurs at night. It comprises two phases, which are plainly distinguished from one another:

A. The initial phase of evacuation, the principal symptoms of which are diarrhœa, vomiting, cramps, change of voice, and alteration in the general appearance of the sufferer.

B. The algid phase, which gradually sets in during the course of the foregoing phase, and which, when it is established, is characterised by various derangements, affecting more especially the production of heat, the circulation, respiration, phonation, secretion, absorption, etc.—derangements which give rise to the striking and characteristic appearance of the cholera patient.

A. Phase of Evacuation.—Diarrhœa.—"Without diarrhœa there is no cholera" (Thoinot). Yet cases

have been recorded, very rarely, it is true, of *dry cholera*—that is, cases in which death occurs with great rapidity, before there has been any evacuation from the intestine.

If the attack has been preceded by the so-called premonitory diarrhœa, the stools immediately assume a different aspect.

If, on the other hand, the onset occurs without premonitory symptoms, the intestine is emptied of its fæcal contents by two or three stools, and the choleraic stools make their appearance.

The typical choleraic stools are serous, liquid, opaline, or greyish white, resembling whey. They hold in suspension whitish flakes comparable to grains of rice, whence the name of rice-form or rice-water stools by which they are known.

These rice-like grains consist of masses of desquamated epithelium, leucocytes, and amorphous debris, resulting from the necrosis of the epithelial cells, and lastly of cholera bacilli, sometimes in enormous numbers.

After centrifugalisation the superincumbent liquid contains a small proportion of albumin.

Sometimes the alvine evacuations are green and bilious, with or without rice-like grains; more rarely they are red, sanguinolent, and dysenteriform in appearance, resembling *meat-scrapings* (Petit, Lesage). In exceptional cases they may consist of a thick mucus, like a thick white soup, or starch paste. Their odour is stale or imperceptible; never fæcaloid. Their reaction is alkaline, rarely acid (Nanu). According to Lesage the stools are at first alkaline, but may become neutral and then acid if the disease persists, and especially if algidity is present. They contain 98 to 99 per cent. of water, little or no albumin, mucin, urea, phosphates, sulphates, etc. They are rich in chloride of sodium and indican. When pure sulphuric acid is added to the stools they assume a characteristic red colour, a true nitrous reaction revealing the presence of indol, known as the "cholera red reaction" (Netter).

The evacuations are very numerous, occurring every

ten or fifteen minutes, sometimes even more frequently, without tenesmus, without effort, involuntarily in serious cases. Although their volume does not exceed forty to fifty centilitres their repetition results in a loss of six to seven litres of liquid in the twenty-four hours (Lorain). The evacuations are less numerous when the cramps become strongly developed; they even disappear completely in serious conditions of algidity.

Vomiting.—Vomiting is less constant and less frequent than the diarrhœa which it immediately follows; it occurs in nine cases out of ten. When it is not present the patient suffers from nausea and eructations: alimentary at first, the vomit becomes bilious, yellowish, or porraceous, with an acid reaction.

Occasionally the vomit is serous, neutral, or alkaline, holding grey clots in suspension, when it rather resembles the rice-water stools. In this case it is known as *rice-water vomit.* Sometimes easy, profuse, and emitted without effort, in other patients vomiting is, on the contrary, difficult, scanty, painful, and even convulsive. It may be accompanied by obstinate and persistent hiccough, and gastric cramps of varying intensity, which are increased by pressure (Gaillard, Lesage). These are often provoked by the ingestion of hot drinks, which the patient tolerates less readily than cold or iced ones.

By reason of the enormous loss of water which they cause the patient, the diarrhœa and vomiting set up a violent and insatiable thirst: six litres or more of liquid are insufficient to assuage it (Thoinot). For the same reason, the mucous membranes of the mouth and tongue become parched and dry. The abdomen, usually soft and yielding, supports palpation without pain, and this palpation causes, above all in the right iliac fossa, a distinct gurgling, as of large air-bubbles, a true splashing sound (Thoinot). Sometimes, however, the abdomen is painful and retracted. There is a complete absence of appetite, and the urine is scanty; while anuria is frequent.

Cramps.—The muscular cramps, which are rarely absent, may be observed in patients whose diarrhœa is not profuse, and even before the appearance of the intestinal flux (Barth, Babinski). They may occur in all the muscles, even the diaphragm (Colliard). They appear first in the muscles of the calf, and then extend to the feet and the hands. In very serious cases they may reach the face, the abdomen, and the thorax. They are rarely generalised. They are spontaneous, and provoked by the slightest exciting cause. Babinski has shown that in cases in which spontaneous cramps are rare or lacking (slight cases, during the abatement of the choleraic period) they may always be provoked by the application of a current of electricity frequently interrupted.

The muscles affected are contracted (Quinquand), hard and rigid, forming distinct prominences under the skin. The pain caused by these cramps is usually violent, and is sometimes absolutely unbearable.

From the commencement of the attack the voice undergoes modifications; its timbre changes, and it grows shrill and hardly audible; the patient's voice has "broken"; the face is emaciated and purplish; the nose is pinched, the eyes sunken, with rings beneath them, and the skin is dry. The temperature, which, at the outset, may have been from 100° to 102° in the rectum and axilla, falls in a little while to 98·4°, 97°, 96°, etc., in the axilla, while it remains stationary in the rectum. The patient's extremities grow colder, and the diarrhœa diminishes or even disappears. The algid or cadaveric phase is now commencing, with the various disorders which accompany it.

B. Algid Phase.—Disorders of Heat Regulation.—After the slight febrile derangement of the initial period hypothermia makes its appearance. The algidity is manifested more particularly in the region of the extremities; it is readily appreciable to the touch. Magendie has noted temperatures of 64·4° and 69·8° at the feet; Lorain has shown that the buccal temperature may fall

as low as 77°. The axillary temperature is less reduced; it is usually between 95° and 98·6°, but has been known to fall to 91·4° (Lorain). The internal temperature bears no relation to the peripheral temperature. Taken in the rectum, it may be subnormal (93·2° Lorain; 89·6°, Galliard; 86°, Hayem), normal, or at times even febrile (104°, Manson; 104·4°, Hayem; 106·7°, Galliard). As death approaches, in the algid phase, the rise of temperature may rise to 107° or more in the rectum or vagina.

Finally, Lesage has recorded three cases in which the rectal temperature fell from 100·4° to 78·6°, while the axillary temperature rose from 95° to 98·9°.

As will be seen, the dissociation between the peripheral and internal temperatures of the cholera patient is subject to no fixed rule.

A survey of the question of temperature from the standpoint of prognosis may furnish us with a few useful indications. A buccal temperature lower than 80·6° is a fatal prognostic. Great differences between the rectal and axillary temperatures, and progressive hypothermia (although this may not be very considerable, nor very persistent) internal and external, are of evil augury; while normal or supernormal temperatures are of good augury.

Derangements of the Circulation.—The pulse is rapid, usually exceeding 100 beats per minute (in a fatal case of Laveran's it was 185). It becomes small and thread-like, and may even disappear completely in serious cases: first from the radial, then from the humeral, and lastly from the crural and carotid arteries. The capillary circulation is interrupted; there is a stasis of the venous system and the arterial system is unduly empty. The heart fails more slowly than the pulse. Its sounds become muffled and remote; the first sound disappears, while the second may be distinguished for some time longer (Magendie). At the very end of the algid phase the ear can no longer perceive anything more than a deep, confused murmur sometimes masked

by a souffle which is attributed to the formation of intracardiac clots (Thoinot).

The blood undergoes profound modifications. Drawn from the veins during life it is black, thick, sticky, reminding one of currant jelly which has not set properly. Its respiratory capacity is considerably diminished. The serum is scanty, and exudes with difficulty; its density is increased, its specific gravity varying from 1036 to 1044 and even 1058; its alkalinity is diminished (Hayem).

There is a relative increase of organic matter, and above all of albuminoids. The chlorides are diminished. The urea is increased, rising as high as 2 grammes ·43 per litre, according to Voigt, and to 3 grammes ·60 according to Chalvet, instead of the normal maximum of 0 grammes ·20. By reducing the mass of the blood to four-fifths of the normal, cholera produces a very great concentration of the blood (Hayem). This is shown by a very considerable polycythemia, the cubic millimetre of blood containing 5,200,000 to 8,000,000 red corpuscles (Hayem). This polycythemia appears early; it commences from the third hour. Anæmia is rare. Cholera is usually accompanied by an early hyperleucocytosis, making its appearance from the twelfth hour; it varies from 13,500 to 60,000 white corpuscles per cubic millimetre, reaching its maximum in the algid phase, and diminishing in the following phase; or, on the other hand, in fatal cases it does not diminish, but will even continue to increase until death. This hyperleucocytosis affects the polymorphonuclear leucocytes (64 to 88 per cent., according to L. Rogers). The proportion of eosinophile leucocytes is diminished or remains normal (0·2 to 1·8 per cent., according to L. Rogers).

Derangements of the Respiration and Phonation.—The cholera patient suffers from a continual dyspnœa, with precordial anxiety and a feeling as of a bar across the stomach, which is stifling him. This dyspnœa is characterised by an increase of the respiratory rate,

which may attain to fifty or sixty per minute, and also by an alteration of the respiratory rhythm. The inspiration is prolonged, and it is not unusual, after a forced inspiration, to observe a pause, followed by a sudden expiration, accompanied by a plaintive moan.

This dyspnœa does not arise from any pulmonary lesion ; it is due to imperfect and insufficient oxidation of the blood, and perhaps also to bulbar excitation due to the cholera toxin. It may, when it is extreme, cause the rupture of a certain number of pulmonary vesicles, thus causing emphysematous lesions.

The voice of the cholera patient, which is merely " broken " in the phase of evacuation, becomes stifled, and, in the majority of cases, there is complete aphonia in the algid phase.

Disorders of Secretion.—During the course of the algid phase of cholera the biliary secretion is diminished (H. Violle) ; the lachrymal and sebaceous secretions are arrested. The lacteal secretion may persist during the attack, as may also the menstrual flow ; but one of the capital symptoms of the algid phase of cholera, and one of the most constant, is anuria : not absolute anuria, but an anuria which is almost absolute. " One may still manage to obtain a few drops of urine, either by waiting, or by searching for the liquid in the bladder with a catheter " (Lorain). As soon as an improvement takes place the urine reappears. However, fatal cases have been recorded in which there was no suppression of the urinary secretion, and other cases in which patients, who for several days had remained anuric, have passed urine a few moments before death (pre-agonal urination).

Disorders of Absorption.—(*a*) Absorption through the mucous membranes of the digestive organs no longer takes place during the algid phase. Food and drink are vomited intact, or found intact in the stomach at the autopsy. Drugs taken are without effect, for they are not absorbed. Opium, sulphate of quinine, belladonna, strychnine, all active medicines, with well-

known effects, are incapable of producing any effect whatever, even in large and almost poisonous doses. Iodide of potassium and ferrocyanide of potassium cannot be detected in the urine (Thoinot). Alcohol, however, appears to be absorbed (Vigla).

(*b*) *Cutaneous and Subcutaneous Absorption.*—"Inunctions of belladonna in the axilla (the dose being 4 grammes) do not dilate the pupils. Bouchut, depositing by incision, in the subcutaneous tissues of algid cholera patients, 5, 10, or 15 centigrammes of morphia, found the doses unaffected at the autopsy. Isambert, in 1866, injected curare under the skin; Grubler injected sulphate of quinine, and Lailler injected atropine; they observed no absorption" (Thoinot).

(*c*) *Intravenous Absorption.*—The absorption of substances injected directly into the circulation takes place in the normal manner.

External Appearances of the Algid Cholera Patient.—The algid cholera patient presents an appearance which is very characteristic. It has been described in masterly fashion by A. Laveran: "The sufferers, exhausted, prostrated, are lying on their backs, their limbs extended, motionless. The eye, sunk in the orbit, owing to the subsidence of the cellulo-adipose cushion, is incompletely covered by the eyelids, for of these the orbicular lid is paralysed (Graefe); dark spots, of a blackish, dirty blue, appear on the surface of the sclera, or the eye is reddened by the development of a keratitis. The cyanosis of the eyelids deeply outlines the osseous contour of the orbit; the nose is peaked; the cartilaginous prominences are seen through the parched skin; the lips are thinned, adhering to the teeth, or half open; they are bluish or purple in hue. The cheeks and temples are hollow; a livid pallor, or a swarthy, blackish tint gives the features an aspect as characteristic as it is appalling, and when, as the disease progresses, the congested, purulent conjunctiva, and the wrinkled cornea, desiccated as that of a corpse, have robbed the glance of all expression; when this withered eye, sunken

in its orbit, shows through half-opened eyelids, it is permissible to say that death has beforehand marked the sufferers with his seal."

The skin of the algid cholera patient presents a cyanotic tint, the intensity varying from blackish purple to pale purple. This is sometimes localised at the extremities (hands, feet, nose, ears), sometimes disseminated all over the body in the form of spots and mottlings, and sometimes general.

This is the *cyanotic* or *blue cholera* which is observed in young subjects who present no renal or hepatic alteration. There is a rarer form known as *pallid cholera* (Giraud, H. Lespiau, and Guerrier), observed in patients who have passed their fiftieth year, or who present lesions which are principally renal, in the course of which the algid patient remains pallid until the moment of death, the moment at which cyanosis generally makes its appearance.

The skin of the cholera patient, and particularly the skin of the extremities, possesses another very special characteristic : it is withered, wrinkled, covered with a cold sweat, viscous and sticky, and gives the sensation of touching the skin of a batrachian.

Sometimes there are veritable sweats of urea.

More or less rapidly the algid cholera patient grows weaker ; his intelligence becomes lethargic, and he presently falls into a condition of torpor, absolute physical and mental torpor. In severe and sudden cases, and above all in cases of blue cholera, the patients are restless and agitated ; they constantly turn over and over in bed ; they are anxious ; they moan and complain, and are slightly delirious. Sometimes the delirium is violent, with cries, and hallucinations of sight and hearing.

Convulsions have rarely been observed at the approach of death, which occurs during the asphyxial collapse. In cases of pallid cholera the patient, calm and somnolent, dies in a state of coma.

The duration of the algid phase varies from a few

hours to three or four days; its average duration is twenty-four hours.

4. The Period of Reaction.—If the cholera patient does not succumb during the attack he enters upon a new period, called by medical writers the period of reaction, which leads to recovery or death.

When the cholera patient recovers, so to speak, at the first trial, without complications, the period of reaction is said to be regular; it is a true normal convalescence.

Such is not always the case, however; and only too often the period of reaction gives rise to complications to which the patient succumbs.

The evolutionary grouping of these complications enables us to speak of *regular reactions*, *abortive reactions*, and *typhoidal reactions*.

The Regular Reaction.—After an algid phase of no great severity, slowly and steadily the patient returns to health. His heart beats more strongly and regularly, recovering sooner than the pulse, which beats more slowly and strongly; and the peripheral circulation re-establishes itself. The skin regains its normal colour; it becomes warm again, first the skin of the forehead, then that of the face, then that of the neck, the breast, and the extremities (Oddo); and it is covered with a warm and abundant perspiration. The respiration grows calm and regular; the voice recovers little by little; the temperature regains its general equilibrium. Absorption through the mucous membranes of the digestive organs and the skin, suppressed during the algid period, reappears in its normal activity, and we sometimes find that drugs taken during the algid period, which then remained inactive, produce their normal effects as soon as the reaction occurs; it is easy to conceive what dangers may result from this in the case of toxic drugs administered without precautions in dangerous doses during algidity (Thoinot).

The biliary, lachrymal, lacteal and other secretions

reappear. The chief indication of the reaction is the re-establishment of the urinary secretion. The urine first emitted is rather scanty, turbid, and more or less albuminous, while it is poor in urea and in chlorides; it contains bile pigments and indican; the sediment is composed of the débris of the epithelium of the bladder, epithelial and hyaline casts, white corpuscles, and sometimes red corpuscles.

The urine of the second emission is more abundant and more limpid. Very soon a state of polyuria sets in, usually reaching its maximum—when as much as eight litres may be passed in the twenty-four hours—between the fourth and ninth days. Lorain, however, has known this polyuria to cease at the end of twenty-four hours, and in other cases to last a month. This polyuria seems to be an energetic means of elimination.

Urea, uric acid, phosphoric acid, and the chlorides quickly increase in quantity, and for a few days exceed the normal. At the same time the urine eliminates waste products from the kidneys and bladder: pus cells, epithelial cells, red corpuscles, casts, crystals of oxalate and urate of lime, etc., etc. The albumin which is constantly present in the first specimens quickly disappears, and as it does so there is often a temporary and unimportant appearance of sugar.

When the reaction proceeds normally it is apyretic, but in certain very rare cases the patient passes very rapidly from algidity to a veritable circulatory pyrexia; the temperature rises to 100° to 103°; the pulse is bounding, its frequency attaining 100 to 120; the urine is febrile, the tongue like that of indigestion, and headache is present. This condition continues for about forty-eight hours; then all becomes normal again, and recovery follows.

The Abortive Reaction.—Aged persons, or subjects enfeebled by some previous cause, physiological or pathological, are more often than not unable to bear the strain of the reaction. The latter sets in, but is insufficient and abortive. The patient remains

prostrate and somnolent; the urinary secretion is scanty; the warmth of the skin does not return in a uniform manner; the hands are still cold, while the trunk is already burning; algidity may return, followed by a fresh abortive reaction.

The patient may succumb suddenly, collapse occurring after several fruitless attempts at reaction; or he may pass into a typhoid-like condition.

The Typhoid State.—The typhoid state gives the patient all the appearances of a typhoid patient; the face is dull and unintelligent; there is intellectual torpor, and more or less violent delirium; the tongue is parched; there is diarrhœa, vomiting, oliguria and severe headache, while the face and the conjunctivæ are injected. Only the temperature—and herein the condition differs from typhoid—remains normal or nearly so (96·8° to 100·4°).

The typhoid state presents many clinical forms, among which we must mention a cerebral form, with its two varieties, the comatose and the ataxo-adynamic, accordingly as stupor or delirium predominates (Oddo), and a gastro-intestinal form, the most frequent, whose chief symptom is an obstinate, bilious, blood-stained diarrhœa, which may cause death between the fifth and eleventh days, by internal hæmorrhage, with prostration and hypothermia. When the patient recovers the convalescence is always long, and is often attended by complications.

In the course of the typhoid state, and also, although more rarely, during the normal reaction, one may observe an essentially polymorphous exanthem recalling those of smallpox, scarlatina, papular roseola, urticaria, erythema nodosum, miliaria, herpes, purpura, etc. These eruptions most frequently affect the extremities, particularly the forearm and the wrist, but may be generalised. Their duration is variable; they evolve without fever, or with slight fever only, and are accompanied by no general derangement; they terminate in a more or less abundant desquamation, according

to the nature of the case. Their prognostic signification is said to be favourable rather than otherwise.

Accidents and Complications

Many accidents and complications may occur during the various phases of cholera. But it is more particularly during the phase of reaction, and during convalescence, that they are most frequently observed. The most important only need be mentioned.

1. **Chronic Diarrhœa.**—The intestine of the cholera patient remains peculiarly susceptible, and tolerates a solid diet with difficulty. A chronic diarrhœa may graft itself on to the cholera and bring the patient into a condition of marasmus.

2. **Gangrene.** — Lesions of the circulatory system are indicated by various complications: anæmia, œdema, or myocarditis, which may result in sudden death. The most usual complication is gangrene. During the algid phase one observes gangrene of a strictly local nature, in superficial patches, on the nose, the tongue (Gendrin), the ears, the lips (Tardieu), etc. But during the period of convalescence and reaction one may meet with:

(*a*) *Visceral gangrene*—rare, it is true, of the intestine (Bouillaud, Mouchet, Oddo) and the lungs (Mouchet, Penieres).

(*b*) *Cutaneous gangrene*, usually subsequent to an irritation of the skin; applications of leeches, blisters, sinapisms, chloroform ointments, etc. Galliard records two cases of sudden and overwhelming septic gangrene following upon subcutaneous injections of caffeine and ether.

(*c*) *Gangrene of the extremities*, usually very serious, due to arterial obliteration, most frequently thrombotic, but sometimes embolic. This form of gangrene usually attacks the foot, but may spread over the whole of the lower limb.

3. Nervous Accidents.—During convalescence cramps may be observed, localised in the calves, and true paroxysms of tetany. These paroxysms, which are not particularly frequent, are localised in the hands or feet; they are generally brief and benign, but occasionally severe and prolonged. The return of the paroxysm may be provoked at will by compressing one of the large nervous or vascular trunks of the part affected (Trousseau's symptom). Localised paralysis has also been reported, and deafness. Dementia of a long-continuing character, and temporary monomania, are not unknown.

4. Pulmonary Complications.—*Pneumonia* and *broncho-pneumonia*, rare in hot countries, are of frequent occurrence in temperate countries, the latter disease being far more frequent than the former (Kelsch, Dubreuilh, Simmonds, Oddo).

Broncho-pneumonia is incidental, more particularly to the abortive type of reaction; its development is insidious and apyretic, the temperature, according to Dubreuilh, varying from 91·4° to 93·3°, while Galliard gives it as 92·5°; it is always subnormal (Oddo).

Pneumonia, according to Oddo, is more obvious in its development; in default of shivering, fever, cough, expectoration, and stitch in the side may attract attention.

These complications are extremely serious, and the rapidity of their development is surprising. Termination by suppuration is not infrequent, and gangrene is not very uncommon.

It has been said that during the algid phase the dyspnœa is sometimes so violent that the pulmonary vesicles are distended to the point of bursting. Usually emphysema stops at the level of the lung, but Galliard has recorded a case in which the air invaded the mediastinal connective tissue, then the subcutaneous cellular tissue of the neck, and finally the supraclavicular region.

5. Jaundice.—This is a rare phenomenon. Most

frequently a *toxic jaundice* of no importance is met with, but sometimes it recalls the characteristics of the dangerous forms of jaundice. In such cases we have to deal with an *infectious jaundice*, caused by the multiplication of the cholera vibrio in the biliary ducts: choleraic angiocholitis and cholecystitis (Galliard, Girode).

6. Secondary Infections.—After cholera, as, for that matter, after all infectious maladies, various inflammations and suppurations and other complications may be encountered. These are: otitis, conjunctivitis, keratoconjunctivitis, parotitis, rhinitis, lymphangitis, erysipelas, boils, phlegmon, thrush, pharyngeal diphtheria, ecthyma, œdema of the glottis, etc.

Relapses, Recurrences

Owing to the results of errors in diet, explainable by the generally voracious appetite and the absolutely inextinguishable thirst presented by the convalescent cholera patient, and sometimes also without any appreciable cause, a relapse may occur which reestablishes the entire series of choleraic symptoms. In all epidemics of cholera a few exceptional cases of recurrences are encountered.

Clinical Forms

From the clinical point of view, cholera presents itself under many aspects, varying according to the development of the disease, the age of the patient, and his previous physiological or pathological condition; lastly, according to the particular epidemic under observation.

A. The evolution of the disease permits of the distinction of several types.

1. Choleraic Diarrhœa, which is the minimum form of the choleraic infection. It is confined to the premonitory diarrhœa which sometimes precedes the attack.

It is difficult to distinguish it, clinically, from simple diarrhœa. Accordingly, in time of epidemic, any case of diarrhœa must be regarded as suspect, and the bacteriological diagnosis of its nature duly established. Choleraic diarrhœa continues for a few days only and ends in recovery.

2. **Cholerine** represents a higher degree of choleraic intoxication. It commences suddenly in the middle of the night, with diarrhœa, accompanied by vomiting, cramps in the calves, severe headache, and intense thirst. There are signs of algidity ; the pulse grows weak ; the urine becomes scanty. Cholerine may terminate in recovery in a few days, but recurrences are common if the slightest error of diet is committed.

3. **Cholera.**—A great many classifications have been proposed for the purpose of grouping the multiform clinical aspects of cholera. A simple clinical division into the slight form, the severe form, and the foudroyant or sudden and overwhelming form is sufficient.

(*a*) *The Slight Form.*—Characterised, apart from the diarrhœa, by the persistence of the radial pulse, and of the urinary secretion, which may be diminished, but is never completely suppressed, and by a barely perceptible cyanosis and collapse.

(*b*) *The Severe Form.*—This is marked by the strongly marked symptoms of cholera already described : aphonia, vomiting, diarrhœa, algidity, pulse nearly or quite imperceptible, absolute anuria, and the choleraic habitus. The reaction is most frequently of the typhoidal type.

(*c*) *The Foudroyant Form.*—In certain exotic epidemics the patients die in a few hours, in a few moments, as though shot or struck by lightning. In our country this foudroyant form, which is often observed in the first cases of an epidemic, is less alarming. Death occurs in three to twenty-four hours (Thoinot).

B. Cholera affected by the Age of the Patient.—Newly born infants fed at the breast usually escape cholera.

In children the progress of the disease is rapid, the evacuations profuse, the vomiting inconstant, while cramps are rare. The child quickly falls into a state of coma and algidity. The period of reaction is particularly rich in nervous phenomena (Thoinot).

The aged are often carried off by foudroyant cholera. Adynamia predominates; the algid phase is abnormally prolonged, and when the reaction sets in it is more often than not abortive. Convalescence is often retarded by gangrenous or suppurative complications (eschars), pulmonary or intestinal.

C. Cholera as affecting the Physiological Conditions of Woman.—Menstruation may persist during algidity. If the menses are suspended during this period, they may reappear at the moment of reaction.

Pregnant women escape abortion only if attacked by the slight form of cholera (Galliard). In at least fifty per cent. of cases cholera causes abortion, and it kills women who do not miscarry even more frequently than those in whom it causes the expulsion of the fœtus (Thoinot).

The expulsion of the fœtus occurs during the period of reaction (Lorain). The child is usually still-born, or succumbs shortly after birth. The death of the fœtus always precedes that of the mother, whence the futility of a post-mortem Cæsarian operation (Galliard). Cholera almost invariably causes the death of women who have recently been delivered.

In wet-nurses the lacteal secretion may fail during the attack, but upon reaction it returns in great abundance. Sometimes it is unaffected, and the breasts may even become gorged with milk, until artificial extraction becomes necessary (Magendie, Oddo, Galliard).

D. Cholera as affected by the Pathological Condition.—Generally speaking, anterior maladies are suspended by cholera; when the cholera disappears they return, completing their course if acute, and prolonging it if chronic.

Bronchitis, pneumonia, acute articular rheumatism,

whooping-cough and diabetes cease at the moment of the attack, to reappear after recovery.

The association of cholera and typhoid fever is one of extreme gravity. The case is equally serious when cholera attacks a malarial patient during an access of fever.

In tubercular cases the pulmonary troubles shrink to a minimum, but if the patient survives the attack the tuberculosis becomes exacerbated and quickly carries the patient off (Briquet and Mignot).

Pleuritic effusions, and the serous or subcutaneous effusions of Bright's disease, of cardiac affections, and of cirrhosis are almost instantaneously swept away by the diarrhœal flux, but the attack is almost invariably fatal to the sufferer.

E. Cholera varies in different Epidemics. — The general physiognomy of the choleraic attack varies from one epidemic to another. In one epidemic digestive symptoms predominate; in another the algid symptoms; in a third cyanosis is the most prominent manifestation. The same is true of the modes of reaction.

Certain epidemics, such as that of Lisbon, have been marked by the extreme benignity of the cases.

CHAPTER IX

DIAGNOSIS

During the course of an epidemic, the rice-water diarrhœa and vomiting, the cramps, cyanosis, the broken voice, anuria, algidity and the peculiar facial aspect of the cholera patient, constitute a body of symptoms which render diagnosis an easy matter.

But this is not the case at the commencement of an epidemic, or when the cases are sporadic ; the clinical diagnosis of cholera may then present great difficulties, for a certain number of pathological conditions present *choleriform* symptoms.

Various acute forms of poisoning—viz. tartar emetic and arsenic—bear such a resemblance to Asiatic cholera that they have been described as *stibial*, or *antimonial cholera*, and *arsenical cholera*. In these forms of poisoning vomiting precedes the alvine evacuations, which are never rice-water. In very acute arsenical poisoning the patient experiences a burning sensation in the mouth, and a pricking in the throat, with a pronounced metallic taste. In poisoning by tartar emetic the sufferer experiences a sensation of burning heat in the throat, which extends all the way down the œsophagus as far as the stomach.

In cases of poisoning by *poisonous fungi* there is rice-water diarrhœa, vomiting, slowing of the pulse, and algidity ; but there are also constant nervous symptoms, myosis, amblyopia, and occasionally strabismus, and paralysis of accommodation. The interrogation of the patient and those about him will direct attention to the cause of the poisoning.

Various forms of poisoning due to *decomposing food* (meat, fish, molluscs, etc.) may give rise to gastro-intestinal symptoms simulating typhoid fever, dysentery, or cholera. Diagnosis is sometimes extremely difficult, even when aided by bacteriological investigations.

Further, infections due to the paratyphoid bacilli, and to Gaertner's bacillus in particular, often closely simulate infection by the cholera vibrio.

The *pernicious algid access* of malarial origin is closely reminiscent of the onset of cholera. But it is preceded by fever, or comes on in the midst of an attack, and the algidity lasts ten or twelve hours at most, never a whole day. The vomit always remains bilious and greenish ; the stools are never rice-water ; the reaction is followed by a sudoral crisis which does not occur in cholera. Quinine is efficacious. Lastly, examination of the blood enables the physician to discover large numbers of malarial parasites.

Certain serious forms of indigestion, certain forms of peritonitis of varying origin, and intestinal obstructions of a medical or surgical order may also make the diagnostician hesitate.

Lastly, it is necessary to establish the exact nature of the first cases of cholera. In the so-called cholera nostras the evacuations are usually bilious or serous. The disease occurs in summer and autumn. From the parasitical point of view it may be caused either by the cholera vibrio, or by a large number of bacteria, the paratyphoid bacilli, *B. coli*, etc.

The reader will perceive the importance which attaches to the determination of the causative agent of a choleriform pathological condition. Only laboratory research can give exact information as to the presence or absence of the cholera vibrio.

In the living cholera patient the vibrio is found only in the stools. It has also been discovered in the vomit. Its presence in the blood (Tizzoni and Catacci) and in the sputum (Mills) should not be admitted unless con-

firmed by further research.[1] At the autopsy it is to be sought only in the intestine: in the rice-water liquid and grains, and the exudate which lines the intestinal walls. If it exists it will certainly be found there, and especially in the small intestine.

The *bacteriological diagnosis* of cholera necessitates several tests: (1) the cholera vibrio must be discovered and isolated; (2) the vibrio must be identified.

1. Search and Isolation.—A rice-like grain is taken, or in default of this a drop of a liquid stool; it is spread out on a glass slide, and after fixation and staining by Gram's method, followed by a double staining by fuchsine (1 in 5), search is made for the incurved rose-coloured bacillus which presents the morphological characteristics of the cholera vibrio. In recent and typical cases these vibrios may be found in pure cultures; in other cases they are comparatively rare, in the midst of a varied and very abundant intestinal flora. Cultures must always be resorted to, together with biological tests in order to identify the suspected germ.

The cholera vibrio being strongly ærobic, it should be sown in wide-mouthed flasks or tubes. The media of culture employed are alkaline, and but slightly nutritive. The simplest medium is peptonised water, prepared according to the following formula:—

Peptone	1 gramme
Sodium chloride	0 gr. 50
Water	100 cc.

After a few hours in the incubator at a temperature of 37° C. a turbidity is produced in this medium, and a slight film forms on the surface, this consisting of various microbes, but principally of the cholera vibrios. A portion of this film is re-sown in peptonised water in a second tube, and from this a third tube is sown with

[1] Greig has recently described cholera vibrios in the lungs and other viscera. They seem to be specially frequent in the pneumonic conditions associated with the disease.—Ed.

the germ, at intervals of six hours. After the third transference the microbic film contains a very large quantity of cholera vibrios, but scarcely any other germs.

Metchnikoff obtains the same result, by adding 2 per cent. of gelatine to the usual peptonised water.

Ottolenghi employs ox bile as a concentrating medium; in this the intestinal germs other than the cholera vibrio do not develop, or develop only with difficulty. This is his formula :

Carbonate of sodium, crystals (10 per cent.)	3 cc.
Nitrate of potassium	0 gr. ·10
Fresh ox bile, filtered through filter-paper	100 cc.

U. Massi sows the stools in a mixture of 1 centigramme to 1·5 centigrammes of ascitic fluid and 4 centigrammes of sterilised water. In this medium the atypical cholera vibrio is said always to attain its characteristic form.

Whatever the concentrating or enriching medium employed, the physician must always proceed to isolate the cholera vibrio. The best method is to sow a particle of the film obtained from the surface of one of the liquid media already described on Dieudonné's agar.

The following is the method by which this agar is prepared :—A mixture is made of equal portions of defibrinated bullock's blood and a normal lye of potassium (56 per 1000) ; it is kept at boiling-point for half-an-hour. Three parts of this mixture are added to seven parts of ordinary agar (3 per 100), neutral to litmus. The resulting mixture is poured into some Petri dishes, which are left for twenty-four hours in the incubator, at a temperature of 37° C. (98·4° F.), or for forty-eight hours at the temperature of the laboratory. The cultivations are made on the surface ; the medium becomes useless five or six days after preparation.

Pilon replaces the potash lye by a solution of sodium carbonate (Na_2Co_3), thus obtaining a medium which possesses the advantage that it can be employed immediately.

On Dieudonné's medium the colonies of vibrios are clearly defined about the eighth or tenth hour. The germs of each isolated colony are then identified. This identification necessitates a certain number of cultures on ordinary agar.

2. Identification.—In order that one may conclude that a given vibrio is the true cholera vibrio, the criteria furnished by the following tests should agree.

(*a*) *Microscopic Examination.*—By this we determine the morphological characters of the bacillus, its motility and the existence of flagella.

(*b*) *The Appearance of the Cultures on Gelatine.—Stab Cultures.*—At 20° C., from the twentieth hour, small irregular colonies appear. A small bubble is quickly formed at the surface, this holding an air-bubble. Liquefaction becomes more pronounced; it progresses funnel-wise, being more marked at the surface than at the bottom of the tube. The air-bubble at the surface continues to exist until the second, third, or fourth day. This is a characteristic culture (but this character is not constant). The liquefaction progressively invades the whole of the culture-tube, always funnel-wise.

On gelatine plates the isolated colonies, at 20° C., after twenty or twenty-four hours, are small, whitish and transparent. At the end of forty-eight hours the gelatine begins to liquefy round them, a little cup of liquefaction forming. The colonies then show a granular centre, surrounded by a ring, which is also granular, but wavy in outline. Around this ring is a third, which is formed by the zone of liquefaction, which enlarges daily until it invades the whole plate.

(*c*) *Test for the Nitrous-indol Reaction.*—This reaction is obtained by adding 1 to 2 centigrammes of pure hydrochloric or sulphuric acid to a twenty-four-hour culture in peptonised water, at 37° C. The reaction is more visible if a small quantity of nitrite of potassium is added to the peptonised water (0 gramme ·10 per 100).

(*d*) *The Agglutination Test with Experimental Serums.*—This agglutination is rather inconstant. There are vibrios which are definitely sensitive to agglutination, but there are others which are only slightly agglutinable. Others again are agglutinable only after being passed through several culture media.

(*e*) *Inoculation.*—The intraperitoneal injection of cultures of cholera bacilli rapidly causes the death of guinea-pigs from peritonitis, with the collection of an enormous quantity of motile bacilli in the peritoneal exudate. If the injection is made into the peritoneum of a guinea-pig which has been highly immunised, the vibrios become immobile, spherical, and granular. The same thing is observed if one injects into an ordinary guinea-pig a mixture of culture and active anti-choleraic serum. *In vitro* Metchnikoff and Bordet have obtained the same results by mixing in sterile test-tubes a diluted anti-choleraic serum, a few drops of fresh serum from a guinea-pig (alexin), and the microbic emulsion.

The majority of these characteristics are somewhat inconstant. The best test for the cholera vibrio is, perhaps, to cause it to be ingested by young rabbits, either by itself or together with microbes which are favourable to its development (Metchnikoff). Of the various laboratory tests employed with a view to diagnosing Asiatic cholera, the sero-diagnosis of Achard and Bensaude and the *fixation of the complement* may be mentioned here. It does not as yet appear, however, that these tests can advantageously replace the bacteriological examinations of the stool.

CHAPTER X

TREATMENT

We have as yet no real specific treatment for cholera. The experiments in serotherapy made up to the present do not appear to be conclusive. Spiro Livieriato claims, however, to have obtained satisfactory results by this method during the Græco-Bulgar War of 1915; including less frequent vomiting, mitigation of the cramps, improvement of the pulse, and palliation of the dyspnœa, the cyanosis, and the algidity.

Practically the only method of treatment which is of recognised value in cholera is the expectant and symptomatic one (Sir Patrick Manson). The first duty to be discharged is to deal energetically with all cases of diarrhœa occurring during the course of an epidemic. All varieties of diarrhœal remedies have been employed, with or without results: opium, paregoric elixir, laudanum, with or without the addition of the sub-nitrate and the salicylate of bismuth, lactic acid, calomel (in massive doses of 5 to 20 centigrammes and more every two hours, until the stools change colour), saturated chloroform water, a mixture of lime, catechu, and opium, etc., etc.

In England and America a remedy known as chlorodyne is much in favour. It is given in doses of four to twenty drops. It is said to be an excellent preparation, but only in cases of premonitory diarrhœa (Navarre, Soulier).

The English formulæ differ as to the composition of this remedy. The product obtained by these formulæ sometimes, in course of time, throws down a precipitate, or even turns into a solid mass, which is useless, the

remedy being administered in drops. The following formula, given by A. Manslau, gives a stable product which keeps well:

Morphine hydrochloride	0 gr. ·50
Chloroform	12 grammes
Alcohol (90 per cent.)	12 ,,
Treacle	*q.s.* to 60 cc.
Fluid extract of liquorice	3 cc.
Atropine sulphate	0 gr. ·05
Essence of peppermint	4 drops
Cherry-laurel water	10 cc.

Mix the chloroform, alcohol, and essence of peppermint in a 60-c.c. flask. Dissolve the morphine and atropine sulphate in the cherry-laurel water, add half the treacle and the fluid extract of liquorice in a mortar, mix, and make up to 60 c.c. with the treacle. Shaken before using.

Various antiseptic medicaments which have been recommended have not responded to the hopes which were founded upon them. Such are salol, iodoform, benzonaphthol, naphthaline, hydrochloric and sulphuric acid "lemonades," creosol, creosote, chlorinated water, creolin, potassium permanganate, etc.

Vomiting may be relieved by means of seltzer water, chloroform water, iced champagne, ice in small fragments, Rivière's draught, etc. The patient should retain a horizontal position, and should drink only a little at a time, as copious drinking usually provokes vomiting.

The beverages most readily tolerated are the "lemonades," made with tartaric or citric acid.

Irrigations of the stomach, with boiled water, plain, or containing 5 per cent. lactic acid, and repeated five or six or seven times a day, recommended by Hayem, Delpeuch, and Lesage, are disagreeable to the patient, and serve to calm him only for a short time.

The cramps are relieved by light friction, dry, or moist, with flannel soaked in essence of turpentine or camphorated alcohol; by hypodermic injections of

morphia ; or, if these means fail, by brief inhalations of chloroform.

In cases of asphyxia Cuneo (of Toulon) has successfully employed inhalations of oxygen.

To relieve algidity, hot bricks have been used; also hot-water bottles, and warm baths (102° to 106° F.). These warm baths, of twenty minutes' duration, repeated every two or three hours, are excellent in cases of average severity. They cause a rise of temperature of 2° to 4°, improve the pulse, moderate or banish the cramps, and favour the secretion of urine (Hayem, Lesage, Siredey, Delpeuch). Semmola gives vapour baths, by means of special appliances, the patient remaining in bed. Injections of caffeine and ether have also been employed.

The rational treatment, however, is that which consists in restoring to the organism a portion of the liquid which it has lost, thereby restoring to the blood the amount of serum which it requires in order to once more become sufficiently fluid to circulate.

As early as 1830 the Russian peasants had conceived the idea of gorging cholera patients with saline water. In 1832, in Scotland, Latta made them drink enormous quantities of saline water. At the same time he gave them enemas of a saline solution, and even injected it into their veins.

At the present time, according to circumstances, one of the following methods of treatment may be employed :—

1. **Enteroclysis.**—Cantani used to make two litres of lukewarm liquid penetrate as far as possible up the large intestine. Lesage, Tipiakov, and Bourcy have obtained good results with this method.

Bourcy injected from two to six litres of boiled water ; cases of average intensity appeared to him to be greatly improved by this treatment. One per cent. tannin may be added to the liquid.

2. **Hyperdermoclysis.** — Subcutaneous injections of artificial serum, the dose varying from 300 to 600

grammes, may be employed in cases of medium intensity, when the circulation is not interrupted.

The injections are made under the skin of the abdomen or the buttock. They may be repeated.

3. Venous Transfusion. — The liquid employed is usually the solution recommended by Hayem :

Sodium chloride (pure)	5 grammes
Sodium sulphate	10 ,,
Water	1000 cc.

The greatest advantage is derived from the employment of serum containing adrenaline.

Other writers employ a solution of 6 parts of sodium chloride in 1000 parts of water, sometimes adding a small quantity of alcohol, but no sulphate of sodium.

Leonard Rogers treated 1000 cases of cholera with only 3·4 per cent. of deaths by intravenous injections of hypertonic saline :

Sodium chloride (pure)	8 grammes
Sodium bicarbonate	20 ,,
Water	1000 cc.

At the same time he administered potassium permanganate internally.

Sir Patrick Manson gives the following formula :—

Sodium chloride	3·5 grammes
Sodium carbonate	3·5 ,,
Boiled water	1 litre

One or two litres of this solution is injected slowly and under slight pressure, at a temperature of 98·4° to 99·4°, into a vein of the arm or leg. The saphenous vein is particularly convenient.

In the most favourable cases intravenous injections positively resuscitate the patient, and cause him straightway to enter upon the period of reaction, re-establishing the circulation, arresting the diarrhœa, and restoring the urinary secretion. Thoinot has described

this effect as resembling *the galvanisation of a corpse, but too often the recovery lasts only a few hours.* Fresh transfusions may be resorted to, if the algidity returns ; as many as two, four, five, and even twelve injections having been administered to the same patient (Lesage). At the present time this method is in current employment, and is not reserved only for cases *in extremis.*

In Hayem's hands it has yielded 30 per cent. of recoveries ; in Galliard's, 29 per cent. It has therefore stood the test of experience, and, according to Hayem himself, " transfusion should be regarded as a regular method of treatment, not as an exceptional method."

During the period of reaction, if the diarrhœa persists, opium and bismuth may be employed. Under these circumstances one may inject into the rectum, according to Sir Patrick Manson, the following solution :—

Tannin	30 grammes
Gum arabic	30 ,,
Warm water	1 litre

Constipation should be treated by means of enemas, never by purgatives.

If the urinary secretion is not rapidly re-established large hot poultices must be applied to the lumbar region, or dry-cupping may be employed ; gentle diuretics should be used with great precaution, and not the active ones, which are unsafe. In convalescents the diet should for some time be of the simplest : milk and water, barley-water or rice-water, thin soups, vegetable soups, meat-juice, etc.

PART II.—EPIDEMIOLOGY AND PROPHYLAXIS OF CHOLERA

CHAPTER XI

HISTORICAL

It was only in 1830 that cholera made its appearance in Europe. But from time immemorial, before it overflowed its accustomed limits, cholera had prevailed, in the epidemic or endemic state, in the valleys of the Ganges, the Brahmaputra, the Nerbudda, and the Tapty. The entire coast of the Bay of Bengal, Malabar, Sumatra, and Cambodia have been the classical homes of cholera. The arrival in these regions of European conquerors, colonists and manufacturers merely increased the spread of epidemics, by bringing them fresh aliment. The conquest of India was marked by murderous losses; soldiers, camp-followers, etc., falling by thousands in a few hours (Graves).

It was in and after the year 1818 that cholera spread beyond its original home, gaining firstly other Asiatic countries, then the Philippines, Mauritius, and the Île du Bourbon. Persia, Arabia, and Syria were soon to become the intermediate countries across which the scourge was to spread, in a manner that was almost periodic, as far as Russia, whence it found its way into the other countries of Europe. From 1830 to 1869 it seemed as though cholera, before overflowing the continent of Europe in formidable incursions, was drawing fresh energies from India. From that year the disease has become naturalised in Europe, and was responsible for terrible episodes, such as those which marked the Crimean War, when the mortality was so

high among the French soldiers and sailors (Fauvel, Scrive). Sometimes it has been possible to trace the manner in which the disease has been transported by Arabs or Egyptians travelling from infected countries, but in reality the disease has become autocthonous, and if it no longer displays the powers of extension which it manifested during the last century, it none the less remains a terrible scourge unless a rigorous prophylaxis is applied.

To give an example of the disastrous severity of cholera, we may recall the epidemic which in October, 1859, attacked the two army divisions of General Martimprey, who was operating in the province of Oran. In a few days more than 3000 men succumbed to cholera.

The menace of cholera, moreover, is always existent; and the military relations which are being established between the East and the West have been and may again become the reason of a fresh appearance of the disease. There are few countries which have escaped cholera: the Faröe Islands, the north of Russia, and Siberia, a few islands in the Pacific Ocean, Terra del Fuego, the island of Nossi-Bé in 1870, etc. This immunity is due to the geographical conditions of these regions, which isolate them and protect them against travellers and the importation of the germ.

European outbreaks have happily become highly irregular and far less extensive. At the present time cholera attacks the army and the fleet, and it also makes its appearance on board ship. Witness the epidemics on board the steamers *Remo* and *Andrea Doria*, sailing from Genoa to South America. The second of these caused 114 deaths among 1357 emigrants.

In India the average annual death-rate from cholera between 1877 and 1886 was 298,000; between 1901 and 1910 it was 380,000, with a maximum of 710,000 in 1906. The average mortality is from 56 per cent. of those attacked (Madras) to 77·8 per cent. (Bombay) (Pottevin).

The Dutch East Indies are not free from the disease

Between the 1st January and the 26th September 1914, 1919 cases and 1030 deaths were recorded.

In Germany the deaths from cholera, which were 114,683 in 1866 and 27,790 in 1875, fell to 866 in 1892, 83 in 1905, and 14 in 1910.

During the Balkan War the third Bulgarian Army, held in check before the trenches of Tchataldja, suffered much from cholera. By the 18th November there had been 17,000 cases and 900 deaths; by the 30th November these figures had risen to 29,626 and 1849 respectively. The number of cases increased more particularly after the men took to drinking river water in which the corpses of Turkish soldiers were drifting. The civil population also was attacked.

In the Turkish Army, during the same period, cholera appeared all the more readily in that it was prevalent before mobilisation among the civil population of Constantinople and the surrounding district, in Syria, etc.

During the present war the French and British armies have had no cases of cholera up to date. There have been very severe and very quickly-developing cases of acute gastro-enteritis, sometimes fatal, but these were found to be due to paratyphoid infections.

On the other hand, the Austrian Army and civil population have been very severely visited by cholera. Between the 23rd September and the 5th December 1914, the official figures for Austria were 3468 cases and 898 deaths. In Vienna, during the same period, there were 386 cases and 39 deaths.

Carinthia, Carniola, and, above all, Galicia have been the scene of numerous outbreaks. During September, October, and part of November, 1914, Galicia numbered 3039 cases and 1164 deaths. In Hungary, during the same period, there were 3605 cases.

A few cases were noted in Silesia among the civil population and the prisoners (277 cases, 33 deaths) between the 23rd September and the 7th November 1914. Bulgaria and Greece were also invaded by the disease.

In Turkey 32 cases and 17 deaths were reported in Constantinople during the early months of 1914; at Adrianople there were 110 cases and 94 deaths among the troops between the 28th February and the 19th May. In the garrison of Rodosto there were 15 cases; in that of Trebizond 14 cases and 12 deaths in January, 1914.

We see, therefore, that the importation of cholera into belligerent nations which it has hitherto respected is within the range of possibility.

CHAPTER XII

ETIOLOGY OF CHOLERA. FAVOURING FACTORS

Caused by a special pathogenic bacillus, the cholera vibrio, cholera is nevertheless not unaffected by *favouring conditions*, some of which are *individual*, while others are foreign, or *extrinsic*.

The comparative protection afforded by childhood is explained by the fact that children at the breast are usually safe from alimentary contagion.

Nevertheless, children of ten months may contract the disease, while, on the other hand, the aged are by no means exempt from it.

It is between the ages of twenty and thirty years, and above all in the male sex, that cholera is most frequent.

No race is safe from its attacks. The black race appears to be even more susceptible than others, and the mortality from cholera is very much higher among them.

No doubt certain individual cases of immunity exist, but they are rare. The effect of agglomerations, wars, and pilgrimages has been invoked; but these factors are operative only because they multiply human contacts—that is, the chances of contamination—and favour the transfer of the bacillus.

Alimentary conditions, such as the employment of raw fruits and vegetables, and indigestible foods, have long been regarded as the adjuvants of infection. Possibly they act simply and solely by transporting the bacillus. But *alcoholism*, acute or chronic, seems to play a more considerable part, for it in-

volves an insufficiency of the digestive and hepatic secretions.

At the time of the Budapest epidemic of 1892–1895, 22·4 per cent. of those attacked were alcoholics; while during the Russian epidemic of 1908, 65 per cent. of those struck down were tainted with alcoholism. This explains why, during an endemic period, we often observe the greatest number of patients on a Monday.

The employment even of pure water in too large quantities may lead to a dilution of the digestive juices, and thereby favour infection.

Excessive fatigue has often been incriminated, not without reason. Its evil effects have often enough been exemplified during military expeditions.

Chronic diseases, tuberculosis, and, above all, inflammation of the intestines, appear to be predisposing factors.

Among the *extrinsic* factors *hot weather* and the summer are most frequently incriminated.

It is certainly a fact that the majority of epidemics are observed during this season. However, epidemics are on record which attained their fastigium in the spring, or even in winter. Such was the Paris epidemic of 1832 (which occurred in winter), that of Berghem (also a winter epidemic), and the Russian epidemic of 1830, when the disease persisted in Moscow during a temperature of 4° F. below zero. The Lisbon epidemic broke out in December, 1893, and the Russian epidemic of 1908 also commenced in winter.

Nevertheless, heat and thundery weather favour cholera, no doubt because of the great consumption of water which they involve.

The following table, borrowed from Bertillon, indicates the duration and the season of various epidemics, as well as the number of victims claimed from the population of Paris.

Cholera becomes localised by election in moist, hot regions, such as the deltas of great rivers (the Ganges, the Nile). In such regions its reign is prolonged, while

in high-lying districts and elevated tablelands it is less persistent. It is observed principally among uncleanly populations, in towns and villages where hygiene is unknown, where dejecta are left lying on the ground, in native quarters, in the *sôks* and suburbs, while the wealthy quarters are frequently spared. The epidemic of Havre, in 1892, attacked the old quarters rather than the rest of the town.

In 1893 the poverty-stricken population of the Îles Molènes and Trielen suffered an enormous mortality.

Year of Epidemic	Date of the first Death Recorded	Date of the last Death Recorded	Duration of Epidemic in months	Seasons during which the Epidemic was most Violent	Number of Deaths attributed to Cholera	Deaths from Cholera per 100,000 inhabitants in each Epidemic
1832. .	Mar. 26	Sept. 30	6 months	{Spring / Summer}	18,402	2345
1833. .	Jan.	Dec.	12 ,,	Autumn	505	64
1849. .	Mar. 9	Oct. 31	8 ,,	Spring	19,615	861
1854. .	Jan. 1	Dec. 29	12 ,,	Summer	8591	732
1865. .	Sept. 1	Dec. 31	4 ,,	Autumn	6357	354
1866. .	July 1	Oct. 31	4 ,,	Summer	5218	289
1873. .	Sept. 4	Nov. 10	2 ,,	Autumn	855	46
1884. .	Nov. 3	Dec. 31	2 ,,	Autumn	986	44
1892. .	Aug.	Dec.	5 ,,	Summer	713	29

In the hamlet of Trielen there were fourteen deaths in six days.

The Budapest epidemic of 1892–1893 manifested itself almost entirely in the dirty and overcrowded houses of the working classes, and among domestic servants out of employment. The epidemic of Les Pouilles, in 1910, presented the same peculiarity (Pottevin).

There are certain cases of individual immunity, revealed by the failure to absorb cultures of the cholera vibrio (Metchnikoff), and owing to this fact certain subjects may escape attack although their dejecta contain vibrios.

The Determining Causes of Cholera

Cholera results from the toxi-infection caused by the cholera vibrio. This infection is localised in the alimentary canal. The germ is most commonly absorbed by way of the mouth and the digestive organs. Having entered the body by the mouth, in one of the ways which will be explained later on, the bacillus reaches the stomach, where the acid secretion is prejudicial to it, but various circumstances, such as the ingestion of the microbe when fasting, or when commencing a meal, or the absorption of a large quantity of contaminated cold water, which flows quickly into the duodenum, and thence into the small intestine, may protect the vibrio from the effects of the acid gastric juice. Having reached the small intestine, the secretion of which is alkaline, and which contains the peptones favourable to its culture, it there multiplies profusely, provoking, at this point, the premonitory diarrhœa.

Such is the first stage of the infection, and to this stage the infection may be confined. More commonly the bacilli sow themselves on the surface of the epithelial layer, and then in its cellular support, and there they cause first desquamation and then necrosis, owing to the toxins secreted. In the dejecta, fragments of the mucous lining, detached and dead, are discovered.

The invasion then spreads along the whole extent of the small intestine. The toxins liberated by the bacilli, and those which result from the death or disintegration of the bacilli destroyed, are absorbed by the large absorbent surface offered by the ill-protected or desquamated intestinal lining. Then it is that the characteristic signs of the choleraic intoxication make their appearance, the most important, for the epidemiologist, being the diarrhœa and vomiting, which are usually profuse.

The dejecta and the vomit contain the vibrio, often in prodigious quantities. *They are, therefore, the*

essential intermediaries of contagion. The first place, however, must be awarded to the alvine evacuations.

These, indeed, often consist of an almost pure culture of the vibrio, mingled with epithelial fragments which give the stools their rice-water appearance, the bacilli swarming in them. Through the breach afforded by the sub-mucous tissue, deprived of its epithelial coating by desquamation, profuse quantities of serous liquid flow, in which the bacilli vegetate. The multiplicity of the stools, their fluidity, and the involuntary emission of evacuations permit of the easy diffusion of these products, which are extremely rich in bacilli. Deposited everywhere, on underclothing, body linen, sheets, the soil, etc., the dejecta carry with them the pathogenic agent. This already explains the excessive contagiousness of cholera.

The bacillus, then, is transmitted principally by means of the choleraic stools: these are the chief source of infection. We shall presently see that cholera carriers are equally contagious, and through the same medium.

The cholera vibrio also exists in the vomit so frequently emitted during the development of a case of cholera, but it is much less abundant there. It is said to have been found in the sputum (Mills),[1] but not in the urine. It does not exist in the blood, intestine, or spleen of the fœtus taken from women who have died of cholera.

The elimination of bacilli goes on during the whole course of the disease, and sometimes even long after recovery.

The spread of the vibrio to the kinsfolk of the sufferer, and those about him, is therefore effected with the greatest facility. For this reason, especially in former years, the mortality among orderlies, nurses, and physicians during epidemics has been enormous. One single sufferer may infect numbers of persons: a village, a town, a continent even. On the 5th July 1854, a ship

[1] Greig's work *loc. cit.* supports this.—Ed.

having landed a cholera patient at the Piræus, the epidemic invaded the whole of Greece. It will be understood how the disease may be transmitted by caravans and shiploads of Mussulman pilgrims returning from Mecca, attacking, on their return, the inhabitants of the countries from which they set out.

This again explains how the great epidemics which ravaged Europe during the nineteenth century spread from India to Russia by way of Persia, Afghanistan, and Arabia, or to Egypt, Turkey, and the ports of the Mediterranean, by means of vessels bringing passengers from the East. Cholera is transported by man, and spreads along the routes followed by man. Countries which have succeeded in isolating themselves entirely have escaped the scourge.

The transmission of the vibrio is effected, not only by admitted cholera patients, but also by persons suffering from " cholerine " or summer diarrhœa (Kelsch). All observers have noted this important fact. Moreover, the experimental absorption of cultures may give rise to these slight forms of diarrhœa (Ferran, Macrae, etc.).

These cases of diarrhœa due to a vibrio, mere cases of indisposition, are extremely dangerous in respect of contagion, for they are not always made the object of special precautions, and, on the other hand, they are able to move about and to travel, thereby spreading the microbe wherever they go.

It has frequently been observed that the great epidemics have been preceded by an unwonted outbreak of cases of diarrhœa or cholerine. Such was the case at the time of the Russian epidemic of 1907–1908. As early as June, 1908, Jacovlev, in Petrograd, noted the increased number of cases of intestinal affections, and of the deaths due to them. Moreover, at this period the bacillus was isolated from the stools of a patient who had recovered.

To sum up: the vibrio is propagated by the *patients* attacked by the *characteristic forms of cholera*; it is also propagated by those who are suffering from *abnormal* or

prolonged forms of the same disease; further, it is transported by those who present only the *morbid symptoms, slight and benign, of simple diarrhœa*, bacteriological examinations nevertheless enabling the diagnostician to isolate the microbe.

But these are not the only sources of contagion. *The vibrio may also proceed*: 1. From *patients who have recovered* more or less recently from one or other of the clinical forms of cholera already indicated.

2. From *perfectly healthy subjects*, who have been in contact with cholera patients, or have absorbed the vibrio, but who nevertheless have presented no morbid symptoms.

Both types constitute what are known as " carriers " of the cholera germ. The latter play a very important part in the propagation of the germ, and they furnish the explanation of the apparent spontaneity of certain epidemics which have affected families, villages, or towns. We ought, therefore, to make a special study of these carriers.

The Carriers of Cholera Vibrios

We have already called attention to a special category of germ-carriers, consisting of persons suffering from slight or insignificant forms of diarrhœa. In practice we must not form any conclusion as to their existence until we have made cultures from their dejecta. Jacovlev, Zabolotny, Zlatogorov, and Kulescha have recorded the presence of the vibrio in subjects who were merely passing liquid stools. In July, 1909, several very grave cases of cholera having appeared in the General Hospital in Calcutta, it was discovered that these cases were due to two natives, who, having the appearance of normal health, but suffering from slight attacks of gastro-enteritis, were carriers of the bacillus.

In patients who have recovered from cholera the vibrio persists in 36 per cent, while the period during

which it may be found varies from two days to two months, and sometimes more (Michailov, Kommelaere, Zlatogorov). The confirmation of this possible persistence of the vibrio in the stools—though these may be normal—of ex-cholera patients was established by Forrest, in India, by Marcovich, in the Trentino (1910), by Franca, in Madeira (1910), and by Defressine and Cazeneuve, in Marseilles (1912). Somewhat exceptionally the persistence of the microbe may exceed a period of 2 months. It may persist for 69 days (in the epidemic of Petrograd, 1908–1909), 90 days (Zeidler), or 100 days (Marcovich).

The labours of Russian and Italian physicians have done much to throw light upon this important point. Montefusca, examining the stools of 107 convalescents, found the vibrio persisting in 60 of these subjects for 15 days ; in 40 it persisted for a period varying from 15 to 30 days ; in 2 it persisted for 35 days, and in the rest from 38 to 78 days. Vanda isolated the bacillus for more than 10 days from 30 per cent. of his convalescents ; for 10 to 20 days from 10 per cent. ; and for 36 to 56 days from 8 per cent. In the case of 24 convalescents who appeared to be rid of the bacillus a slight purgative caused its reappearance in 3 of the 24. The administration of a purgative (15 grammes of magnesium sulphate), recommended by Zirolia, sometimes enables the physician to discover that the disappearance of the germ is only apparent. On the other hand, an attack of indigestion or an alimentary excess may produce the same result.

Other investigations made in Italy on over 3000 healthy carriers of the bacillus showed that 50 per cent. of the carriers no longer carried the vibrio after five days ; 77 per cent. of the other carriers revealed the germ on the tenth day ; and 95 per cent. on the twentieth day (Pottevin).

Baldoni examined, at Brescia, between the 5th of August and the month of December, 1915, 5200 fæces passed by soldiers under treatment or in quarantine.

He found that 2·5 per cent. of the latter were carriers.

There is no longer any doubt that certain persons are capable of retaining the vibrio for considerable periods. The designation of "chronic carriers," although it represents a rare eventuality, denotes the existence of these cases. Cases of long-continuing diarrhœa have been noted in which the microbe has persisted for a period of six months (Alain, Vallée and Martineau, Ruffer), a year, and even three years (Crendiropoulo and Panayotatau).

Analysing the researches conducted by the preceding writers, and also by Piras, Debonis, Defressine and Cazeneuve, Necchi and Randone, etc., it follows: (1) that the cholera vibrio may persist after the complete recovery of the patient in about 30 to 33 per cent. of cases; (2) that this persistence is not, as a rule, very prolonged, but continues at most for thirty or forty days, rarely more; (3) that the excretion of the vibrio may be irregular, intermittent and interrupted for a few days, and then reappears.

From this last point of view the facts are analogous to those which have been established in respect of carriers of the bacillus of typhoid, but the long persistence of the latter bacillus, which may continue during a lifetime, does not obtain in the case of the carrier of the cholera vibrio.

In practice it is always useful, before concluding that the vibrio has disappeared, to make repeated cultivations and previously, on each occasion, to administer a gentle saline purgative.

The existence of healthy carriers—that is, carriers who have never suffered from cholera, even in an obscure or attenuated form—is to-day fully demonstrated. The truth is that there are carriers whose blood contains antibodies, which shows that the choleraic infection must have been serious. Klein, who frequently isolated them, owing to this observation, queried the specific and pathogenic character of the vibrio described by

Koch. Persons who, in time of cholera, absorb the vibrio but escape infection, possess, in reality, only a relative immunity. Their existence has been verified by many writers during epidemics, and in various countries. In Russia Jacovlev found that in 100 instances of isolation, the bacillus was in twenty cases derived from healthy subjects. At the time of the Russian epidemic, during the three months commencing on the 21st December 1908, the stools of 2440 persons who had been in contact with cholera patients were examined. The vibrio was isolated 125 times, or in 5 per cent. of these cases.

These carriers fell into three groups :

1. Twenty-five were in the incubation stage of cholera.[1]

2. Forty were emitting rather liquid stools, without morbid symptoms.

3. Sixty *exhibited normal stools*, and presented no sign of disease.

According to more extensive data published by Jacovlev, Zlatogorov, and Kulescha, the examination of 21,962 persons yielded the cholera vibrio 4497 times. Of 9752 persons who had been in contact with cholera patients 571 were carriers of the bacillus.

The proportion of these healthy carriers among those who form the entourage of cholera patients may vary, however, within wide limits. The average proportion is 6 to 7 per cent. (MacLaughlin, Forrest). Such carriers have been found among pilgrims on their return from Mecca (Zonchello). They were also found on the occasion of the epidemic which visited Holland in 1909 ; in the Belgian epidemic (Van der Velde), the Marseilles epidemic of 1912 (Salimbeni and Dopter, Orticoni), the Italian epidemic (Vivaldi), and the epidemics in Madeira (Franca and Stevens), and Tunis (Conor). The

[1] Cholera made its appearance one to three days later. We have here the confirmation of the idea that the cholera subject may be contagious *before* the appearance of the first symptoms of cholera (Edm. Sergent, L. Nègre, Bregeat and Vivien).

proportion of carriers may be very high—as high as 14 per cent. (as in the Genoa epidemic of 1911, when of 1525 persons 214 were found to be carriers). On the other hand it may be very low, or the carriers may be non-existent. Crendiropoulo, examining the stools of 34,461 persons in Egypt, isolated the vibrio from only 25 of them. At the time of the Madeira epidemic not one of the seventy-one physicians or nurses was found to be a carrier. It results from this that a thorough prophylaxis may prove to be a perfect protection against infection by the vibrio, whether latent or effective.

It has been queried whether the vibrios thus isolated from the dejecta of healthy carriers have pathogenic properties. Attempts to inoculate animals have sometimes proved their low degree of virulence (Piras), and sometimes their activity and toxicity (Debonis, Cimmino, etc.).

The period during which the germ-carrier eliminates the cholera vibrio is fairly brief, varying from a few days to three weeks.

Between the 4th of December 1908 and the 4th of December 1909 the Service of Hygiene in Petrograd examined the fæces of 9357 subjects who had been isolated as possibly contaminated. Of these 577 were carriers of the vibrio. Between the 4th of December 1909 and the 4th of December 1910, 3173 persons exposed to contagion through their proximity to cholera patients were examined in the same way. The results were :

Adults . . .	2368 . .	157 carriers =	6·6 per cent.
Children, 1 to 15 years	720 . .	71 ,, =	9·8 ,,
Children under 1 year	85 . .	17 ,, =	20 ,,

(Pottevin). Children, accordingly, are particularly dangerous.

In connection with the cholera in Hedjaz, it has been noted that the pilgrims, who yield so many cases of the disease, also exhibit instances of healthy carriers. In 1912–1913, 2·8 per cent. of the pilgrims had agglutinable vibrios in their stools.

It was in the Egyptian hospitals that the discovery of suspected vibrios was first made with any frequency. In certain cases of ulcerative gangrene of the intestine a vibrio identical with that of cholera was isolated. In 90 post-mortem examinations suspected vibrios were discovered in 36 instances: some of these being extremely virulent, agglutinable, secreting a hæmolysin, etc.

In subjects returning from Mecca and dying of various diseases (such as dysentery), cultures have yielded a vibrio (the vibrio of El Tor) analogous to the cholera vibrio, agglutinable by anti-choleraic serum, and showing Pfeiffer's reaction. Nevertheless, it seems that we ought to regard these bacilli as paracholera vibrios. Castellani has isolated paracholera bacilli in Ceylon.

The important part played by the carriers of bacilli in the extension of epidemics of cholera need not be emphasised. The perennial nature of the disease in certain countries, its persistence, and its periodical or irregular return in others, can only be explained by the persistence of the germ in certain persons who act as reservoirs or depositories. A healthy subject, travelling through a given country, or sojourning in it awhile, may thus become the origin of serious epidemics.

. . . . . .

The conditions which thus permit of the conservation and retention of the cholera vibrio, during a variable period, by a certain number of persons who have or have not suffered from an attack of cholera, are the same as those which obtain in the case of carriers of the bacillus of typhoid, or the paratyphoid bacilli. The cultivation of the contents of the gall-bladder on the occasion of autopsies on victims of cholera first enabled Nicati and Rietsch, during the Marseilles epidemic of 1884, to isolate the comma bacillus. This important discovery was verified by Tizzoni and Cattani, and by Doyen, Raptchevski, Sevastianov, Rekovsky, Tanda, etc. The vibrio is not, as a matter of fact, absolutely constant in the gall-bladder; but its occurrence there is frequent, since

Brullov found it in 76 per cent. of cases, and Otto Schöbl, in the Philippines, in 18 cases out of 39.

Kulescha concluded, after conducting 430 autopsies, that the vibrio is most frequently encountered, first in the intestine, and then in the gall-bladder. As in typhoid infection, the local multiplication of the vibrio determines catarrhal and hæmorrhagic lesions of the mucous membrane of the gall-bladder, sometimes amounting to a true cholecystitis. The same microbe may give rise to suppurative angiocholitis, with jaundice (Piras). During the epidemic of Toulon (1911) Defressine and Cazeneuve found the vibrio in the pure state in the bile of three patients who had succumbed to cholera, the cultivations having been made four to eight hours after death.

As regards the bacteriological diagnosis *post mortem*, therefore, the search for the vibrio in the bile may be of great service; but it should be undertaken in good time.

Experimentally, Baroni and Ceaparu have discovered the existence of the vibrio in the bile of inoculated rabbits. Job has observed that if the guinea-pig is made to absorb the vibrio it may be found in the blood, in which it remains for a short time, and then in the gall-bladder. He believes that the intestinal phase of cholera is preceded by a septicæmic phase.

Otto Schöbl has observed the brief survival of the vibrio in guinea-pigs inoculated in the gall-bladder, the stomach, or the intestine. Intravenous injection is more favourable.

However this may be, the passage of the bile into the intestine explains the presence of the vibrio in the dejecta of carriers.

It is, therefore, through the medium of their excreta that the carriers of vibrios, like those suffering from cholera, disseminate the bacillus and become contagious. The contagiousness of the carrier is inferior to that of the actual cholera patient, because the number of bacilli eliminated by the former is very much smaller.

CHAPTER XIII

ETIOLOGY OF CHOLERA—*continued*

The Modes of Propagation of the Cholera Vibrio

Issuing from the cholera patient, or from a carrier of the bacilli, the cholera vibrios contained in the dejecta proceed to contaminate linen, chamber utensils, latrines, privies, the soil, water, etc. They may be transferred by the sufferer or the carrier to those who attend on him or surround him; the contagion is in that case *direct.* They may on the other hand be propagated by one of the intermediate agencies mentioned below: the contagion is then *indirect.*

Innumerable examples testify to the propagation of the cholera bacillus from man to man. Examples of the direct propagation of the vibrio by germ-carriers have also been published. In families and collections of people, persons whose duty it is to prepare food (cooks, etc.), when they are germ-carriers, are particularly dangerous. At the time of the Petrograd epidemic a female cook in a house of retreat who had prepared a dish with gelatine contaminated forty-seven persons thereby. Kulescha has recorded the case of an old lady who, having a terrible dread of cholera, used to have her crockery boiled, and her food sterilised, while she frequently disinfected her hands and employed only boiled water for her bath. None the less she contracted cholera, of which she died. Inquiry proved that she had been contaminated by her bacilli-carrying cook, who lived in a neighbouring house, and had been in contact with cholera patients.

W. Greig records that an epidemic which broke out in the prison at Puri, in India (1912), was due to

the communication of the infection by a vagrant who had previously suffered from cholera. Imprisoned on the 25th July, a few days later he had caused seventeen cases among the rest of the prisoners and the warders. There were five deaths. His dejecta contained numerous vibrios.

There is, therefore, a useful comparison to be drawn between the modes in which cholera is transmitted and those by which typhoid fever and the paratyphoid fevers are transmitted. *Cases of infection by contact are in reality cases of infection by means of dirty hands*, the hands of the person who transmits the germ and contaminates other persons, or the hands of the person who is infected, and contaminates himself, by neglecting to wash his hands.

It is easily understood that direct contagion readily occurs in working-class circles, in country districts, and among the natives of non-European countries, because the general conditions of hygiene and cleanliness are less regarded there.

The original centre of contagion being in fæcal matter, we may well ask ourselves what becomes of the vibrio, and how long it can survive—that is, remain contagious. We know that according to R. Koch and certain others the vibrio is supposed not to persist longer than twenty-four hours in the dejecta. But investigations made by Mattei and Canalis have shown that in putrefying, and therefore alkaline dejecta, the bacillus may survive for two or three months. Filov found that it persisted from 18 to 101 days; Rabescha, for 9 months. It is in fæcal matter, sheltered from the air and the light, that the vibrio persists longest (Zlatogorov). Job, having during the winter mingled cholera vibrios with fæcal matter, made cultivations every three days in peptonised water, peptonised and saline agar, etc. He found that the bacilli persisted for 4 to 33 days.

Investigations as to the persistence of the vibrio in various media give the following data:—In moist sand,

7 days; in moist garden soil, 33 to 68 days; in moistened dust, 4 months. Investigations as to its persistence on the surface of a great variety of foodstuffs give the following results:—On barley bread, 1 to 3 days; on ordinary bread, covered up, 7 days; on smoked herring, 4 days; on meat, 8 days; on fruits and salad, 2 days; on fresh apples, cut, 4 days, etc. In reality the nature of the substratum matters less than the conditions of dryness or humidity, the action of light and of the oxygen of the air, and the degree of acidity of the medium, which affects the vitality of the bacilli. During the sojourn of varying length which the vibrio makes in the outer world while incorporated in fæcal matter, it is, as a rule, imperfectly protected. In reality it offers little resistance; desiccation kills it in 3 or 4 days, or at most in 13 to 38 days (Kitasato). Antiseptics and acids kill it quickly.

One may conclude, in consequence (1), that apart from immediate or direct transmission, the cholera vibrio is transmitted by means of indirect or intermediate factors of transmission: *by all the extremely various intermediaries on which the alvine evacuations of cholera patients or the dejecta of carriers may be deposited.*

2. *That its conservation will be the more readily effected as the receptive medium is more humid,* and better protected from the microbicidal action of light and the oxygen of the air.

3. That as desiccation has the effect of killing the bacillus, its propagation by means of dust is hardly probable, and would at best be greatly restricted.

4. *That contaminated articles of food, especially liquid food, are contagious factors of the first order.*

The intermediate agents which may serve to propagate the cholera vibrio are either living and animated, or inert. Both play a more important part than that of direct contagion in all localities subjected to a thorough personal hygiene. This is why it was said that direct infection, or infection by contact, "played only an insignificant part in the hospitals of Petrograd,"

although in these hospitals the cholera patients were very insufficiently divided from the other patients. We must therefore award an important place to indirect contagion.

This is commonly effected by means of *flies*. During the hot season, at the period of their chief activity, the part played by flies is a considerable one. The vibrio lives in the alimentary canal of the fly. Maddox has verified its presence in *Calliphora vomitoria* and *Eristalis tenax*. Savtchenko, having fed flies upon cultures of the cholera vibrio, found the vibrio in a pure culture in their intestines. Ganon, similarly, verified its presence 20 hours after an infectious meal. According to Passek, the vibrio lives 72 hours in the fly's intestine.

Tizzoni and Cattani have isolated the bacillus from flies captured in the rooms of cholera patients. Tiskov and Tsukuki have done the same.

Flies alight upon the vomit or excrement of cholera patients, thus loading themselves with vibrios, which they absorb, or with which they soil their feet and legs. They defæcate very frequently, depositing the specific infection upon all sorts of articles of food—fruits, sweets, cakes, custard, pork, bacon, etc. Lastly, they pollute the face and hands of sleeping children and adults. The bacillus survives for several days on the surface of most articles of food.

The vibrio does not live long on cut fruits whose juice is acid. It survives longer on very ripe fruits, on the melon, the grape (3 to 4 days), and the date. Putrefaction and mould, etc., have little effect upon its vitality.

Often enough the flies die within a few days; their dead bodies then may fall upon food and pollute it. This is why the proximity of kitchens, dining-rooms, mess-rooms, tents, larders, slaughter-houses, pork butcheries, butchers' shops, pastry-cooks' shops, etc., to privies, stables, accumulations of dung or organic refuse, or to hospitals, may in seasons of epidemic entail the most serious danger.

Flies, moreover, may cover long distances, being transported by carts, carriages, railways, and ships.

The pollution of food may be effected not only by flies, but, as has been said, by cholera patients and by germ-carriers, by the soil, and by water (as in the case of raw fruits and vegetables).

Cases of contagion have been reported which were due to polluted clothing, especially to linen (shirts, sheets, etc.). The calling of washerwoman in a special manner exposes those who follow it to infection by cholera vibrios. Duflocq has published examples of these various modes of contagion. The cholera bacillus multiplies on the surface of a piece of soiled linen which has been folded up. Its period of vitality is from eight to twelve days on damp stuffs, and one to four days on dry fabrics. On damp cloth, protected from the air and the light, it may survive for five weeks (Gamaleia).

Contagion by means of footgear may be compared with the foregoing means of contagion. It occurs on soil which has had dejecta thrown upon it, or in gardens, or ill-kept privies, etc. The germ is thus introduced into the dwelling-house by the boots or shoes, or by wooden shoes or clogs, or by bare feet even in country districts. It thus becomes deposited on the hands, or on the floor, whence it is picked up by flies, or by children at play. This is one of the ways in which the cholera microbe may be introduced into the organism. It must, of course, reach the mouth. This it may do in a great variety of ways.

The infection of the soil may also be effected by means of the bodies of the victims of cholera, which carry with them a stupendous quantity of pathogenic germs. In them the bacillus may survive for twenty-eight days. In India the religious practice of the natives, who place the corpses of those who have died of cholera on the banks of the Ganges, favours the infection of the water of the river.

The same microbe which, mixed with the dejecta of

cholera patients or germ-carriers, pollutes the surface of the soil may also contaminate vegetables and fruits which have fallen from the trees. According to Remlinger and Nouri, fish living in contaminated water may preserve the vibrio intact. It may survive within the fish for two to four days (Gran and Shor).

Infection by water holds the first place in the propagation of cholera, as in that of typhoid fever.

The cholera vibrio retains its vitality in water for considerable periods (Nicati and Rietsch, Straus and Dubarry). Investigations undertaken to elucidate this point have yielded results which are not absolutely concordant. According to some the microbe may live for thirty to eighty days in well or river water, while, according to others, it can only live for seven days (Santi Sirena, Dunham, etc.). It is possible that the cholera vibrio not only survives, but even undergoes multiplication in still waters, when it is sheltered from the light and when the external temperature is sufficiently high.

Hankin, however, has called attention to the fact that the waters of the Ganges, and of its affluent, the Jumna, possess bactericidal properties in respect of the cholera bacillus. Filtered water in which vibrios had been placed, and which was subjected to bacteriological examination, yielded, at the outset, 7000 to 8000 colonies, but was sterile at the end of three hours. This property disappeared on boiling. To tell the truth, it appears to be exceptional.

The effect of solar light on water, even when diffuse, has a powerful bactericidal effect. Clear water, holding the cholera vibrio in suspension, and exposed to the rays of the sun, is sterilised in three to four hours. In hot countries those waters which are sheltered from the solar rays, such as the water of ponds, and of the Indian tanks, are particularly dangerous. The renewed contamination of water by the introduction of dejecta, the washing of the underclothes of cholera patients or germ-carriers, the discharge of contaminated brooks

or tributaries into a river, form many causes of the persistence of the infectious germ.

The causes of the contamination of water-supplies by the bacillus of cholera are indeed extremely numerous. The rains favour the direct discharge of dejecta, of putrid liquids, of contaminated manure-pits, into rivers or bodies of standing water. The subsoil layer is exposed to the same infection, through the infiltrations which reach it, and which originate either on the surface (owing to the spreading of fæcal matter on the soil) or at a deeper level (from cesspits).

The bacilli constantly swept down, in times of epidemic, by rain-water, sewage, the washing of linen, etc., maintain the noxious condition of water-supplies. In the Ganges the water of the river itself does not immediately kill the bacillus. The religious practices of the Hindus, which prescribe baths and ablutions in the sacred river, and the ingestion of the water into which corpses are thrown, are in the highest degree favourable to infection.

The direct proof of the presence of the cholera bacillus in a large number of suspected rivers was obtained long ago. Nicati and Rietsch isolated it on several occasions from the waters of the Old Port of Marseilles. Sanarelli, Metchnikoff, Netter, Vincent, etc., have also verified its presence in different waters. At the time of the epidemic which prevailed in Petrograd in 1908, 1010 samples of the water of the Neva yielded the vibrio 193 times. In the same water when filtered, which serves as drinking-water, the bacillus was found in 13 per cent. of the specimens analysed; and in 6·1 per cent. of the specimens of ice examined. The investigations undertaken by Zabolotny and his colleagues resulted in the isolation of the vibrio from 549 of 3505 samples of water.

Huylov isolated the vibrio from the water of the Volga. In this water the vibrio persists for 508 days, a fact which can only be explained by its actual multiplication. River-mud is a receptacle favourable for

the preservation of the microbe, and the stirring up of the mud has been incriminated as the cause of the contamination of river-waters.

The muddy bottoms of wells are said to possess the same property. Defressine and Cazeneuve have isolated the vibrio from the mud of a river.

Similar discoveries have been made in all countries, notably in Italy. One must suppose that the specific contamination of water, and especially of river-water, is maintained by the dejecta of the carriers of germs.

Epidemiology, as a matter of fact, confirms at every point the etiological rôle of drinking-water in the propagation of cholera. This rôle is an important one. At the time of the epidemic which prevailed in France in 1884, Marey, in his well-known report to the Academy of Medicine, demonstrated with remarkable precision the influence of this factor, describing epidemics in certain districts or villages which were attributable to the absorption of contaminated water, the disease spreading through the different villages strung out along the same water-course. A sufferer brought the germ to the hamlet of Val, in the canton of Vignolles. His linen was washed in a wash-house from which the water drained into a little river flowing on to Montfort. At Montfort there was a case of malignant cholera.

At Barrême the contamination was due to the clothes of a working man suffering from cholera, which were thrown into the River Asse. All the villages downstream had cases of cholera. At Gap, Prades, Cerbère, Perpignan, Nantes, etc., the same thing was proved to occur.

The Hamburg epidemic commenced on the 18th August 1892. By the 29th there had already been 3400 cases and 1100 deaths, due to the water of the Elbe, which was unfiltered, but was the only water utilised. The city of Altona, which adjoins Hamburg, was very little affected. In these two communities it happened that one side of a street, belonging to Hamburg,

was infected, while the other side, forming part of Altona, was unaffected. In 1913 there were, on certain days, in Hamburg more than 1000 cases a day. In Altona, where filtered Elbe water was consumed, there were only sporadic cases.

The Petrograd epidemic of 1908 was due to drinking-water. There were as many as 400 cases daily (Gamaleia).

The epidemic which prevailed in the outskirts of Paris in 1892 afforded another demonstration of the influence of drinking-water. Neuilly, Suresnes, Saint-Denis, which were supplied with water drawn from the Seine below Paris, suffered severely. At Saint-Denis those inhabitants who employed the water from an artesian well were unaffected (Netter).

The contamination of river and lake water is certainly effected by sewage and the washing of clothes. But boatmen, bargees, etc., play a very important part in infecting such waters; for they are frequently infected by drinking them, and they themselves discharge great quantities of germs into the water if they are sick of cholera or carriers of the vibrio.

The presence of a certain amount of marine salt is by no means prejudicial to the preservation of the vibrio in water. Quite the contrary, the salt favours its multiplication, which is a point of great interest, and explains the persistence of the bacillus in the estuaries of rivers. At Archangel the water of the Dvina has been found to be thus contaminated. We know, on the other hand, that peptonised and saline agar is one of the best media for the isolation of the vibrio. According to Parini, sea-water does not kill the microbe. He mentions the case of two men who, at a time when no epidemic existed, contracted cholera as the result of falling into the polluted water of a harbour, when they swallowed a certain amount of water. Sanarelli, Carapelli (at Palermo), etc., have insisted on the comparatively frequent occurrence of vibrios resembling the cholera vibrio in river waters,

apart from the existence of any case of cholera. There is no doubt as to the animal or human origin of these microbes. It is, nevertheless, curious that the existence of these microbes is not accompanied by a simultaneous choleraic infection. Zlatogorov has recorded the case of a Russian student who, having accidentally absorbed a bacillus isolated from the Neva, developed a choleriform infection. But on the other hand, E. Sergent and L. Nègre have recorded the immunity of a town whose fluvial waters contained a vibrio which apparently was the authentic cholera vibrio. There are still, therefore, some unknown vibrios.

Gosio has expressed the opinion that earth-worms, which are coprophagic, might contribute to the propagation of the cholera vibrio. He has found the vibrio in the alimentary canal of earth-worms. These vibrios came from a lake from which Carapelle had isolated the cholera bacillus. A month later the bacillus still existed in the intestine of young earth-worms. According to Venuti, earth-worms and molluscs retain the vibrio in their alimentary canals, but it becomes attenuated.

The danger of consuming raw oysters and other shell-fish results from the fact that these molluscs have lived in waters infected by the cholera vibrio, while preserved in the neighbourhood of ports or near the outfall of sewers. Oysters feed on particles of organic matter contained in the water. In this way they retain its impurities; they act as a kind of filter, conserving the vibrio for twelve to sixteen days (Pinzani). Cases of established contagion, due to oysters (Geddins, Calmette, Rouchette, Pottevin, etc.) have been reported in Italy and in France.

Fish living in contaminated waters may introduce the germ into the body if they are eaten raw, or insufficiently cooked, for example, as in Japan.

The transportation of the microbe has also been attributed to the bilge-water of ships, which may contain the germ. It has been stated that sea-water is by

no means hostile to the vibrio. Nicati and Rietsch, having stirred the vibrio into sterilised water taken from the Old Port of Marseilles, discovered that the microbe survived for eighty-one days. Other observers have noted its persistence for two or three weeks, and even for four months (Piccinini). In 1909 the bacillus was isolated at Gand from the very saline bilge-water of ships hailing from Riga and Petrograd. Water employed as ballast may also contain the vibrio (Jacobsen, of Copenhagen). According to Remlinger, the spray of contaminated sea-water may spread or communicate the cholera vibrio.

It goes without saying that if the drinking-water kept on board ship contains the cholera bacillus, it may become the point of departure of an epidemic among the sailors, and in the ports at which the vessel touches, or in towns or villages situated along the course of a river. The epidemic which prevailed in Toulon in 1911, attacking the crews of the warships there, was attributed to this cause (Defressine and Cazeneuve).

With the exception of milk, the part played by beverages—wine, cider, beer, etc.—is inconsiderable. The cholera vibrio is not robust, and is easily killed in an acid medium, such as wine. It does not survive longer than five minutes in red or white wine, mixed with an equal volume of water. In beer it survives only for a few hours. Vinegar and lemon juice destroy it very quickly. According to Metin, infusions of tea, if contaminated, may transmit the vibrio.

Milk has often been condemned as a source of infection. Its pollution may result either from dilution with polluted water, or to contamination by a milkman or milk maidwho is suffering from cholera or is a germ-carrier, or to the use of unclean receptacles, or, lastly, to flies, living or dead. We have already spoken of the infection of milk by means of flies.

Le Dantec has recorded the details of an epidemic in which nine sailors out of ten contracted cholera after

drinking milk diluted with water from a pond into which the dejecta of choleraic subjects had been thrown.

The vibrio, as a matter of fact, multiplies in milk, above all in boiled milk. The lactic ferment is injurious to it and kills it. It readily survives on the surface of butter, in fresh cream, and on cheese.

CHAPTER XIV

PROPHYLAXIS OF CHOLERA

Prophylaxis of Favouring Causes.—Although the factors which have been described as favouring causes play only an accessory part, their importance must not be disregarded in times of epidemic.

A moderate diet and sobriety are useful precautions. Heavy meals should be avoided, and the excessive use of alcohol. Purgatives may awaken the choleraic infection.

Personal cleanliness, particularly that of the hands, is to be especially recommended. Avoid fatigue, over-exertion, and long marches, especially in the heat of the day, as these factors diminish organic resistance and increase thirst, thereby augmenting the possibilities or the severity of contagion.

Houses, courtyards, and gardens must be kept scrupulously clean, the same applying to barracks. Ventilation, natural lighting, and sunlight are excellent means of disinfection.

Particular attention must be paid to closets, privies, urinals and dung-hills, which ought to be removed, and manure-pits, which must be done away with.

Kitchens are to be inspected, and everything should be destroyed, by fire or burial, which might attract flies and permit of their multiplication : ordure, kitchen refuse, organic matter, etc.

When there is a danger of cholera the general hygiene of towns demands the same measures. The accumulation of filth must be avoided ; the flushing of gutters and sewers must be facilitated ; streets, cesspools, etc., must be cleaned. Slaughter-houses, butchers' and

pork-butchers' shops, factories, and the working-class quarters should be carefully inspected. Sanitary inspectors should visit hotels, restaurants, and wine-shops, above all in the neighbourhood of ports and in insalubrious quarters, and ensure that the special preventive measures which will presently be described are applied.

In the case of barracks, the entire premises should be kept in a condition of scrupulous cleanliness. Scrubbing and sluicing with plain water, which favours the conservation of the microbe, is to be abandoned in favour of cleaning by means of sawdust impregnated with an antiseptic (carbolic acid, lysol, cresol).

Dung-hills or muck-heaps must be removed from the barracks daily, while dung-pits should be cleaned out and sprinkled with antiseptics. It is useful to appoint fatigue parties to clean the latrines or privies and their approaches several times a day.

Prisons, reformatories, etc., whose cleanliness only too often leaves much to be desired, must not be neglected. In camps, and in time of war, the application of the above measures must be most strictly enforced.

It is also necessary to eliminate from the diet all indigestible and imperfectly cooked foods, salt pork, fresh pork, sausages, meat pies, etc., which might be made from unwholesome meat.

Raw vegetables are to be prohibited: salads, radishes, cucumbers, tomatoes, etc., and even raw fruits. River bathing must be stopped.

Prophylaxis of Cholera on board Warships.—The prophylactic rules to be followed are obviously the same on board ship as on land. Respecting vessels on active service, a circular issued by the French Ministry of Marine on the 3rd October 1909 prescribed the following measures: Healthy vessels touching at an infected port will cast anchor at a sufficient distance, will reduce the term of their stay in port, will avoid mooring at quay-sides, and will take the usual precautions with a view to avoiding infection.

Infected vessels will, in respect of themselves and their sick, take the necessary measures of isolation, disinfection, etc. On their arrival they are subjected to the medical inspection of crew and passengers, the disinfection of dirty linen, water-closets, etc., the immediate disembarkation and isolation of the sick, and also of the healthy passengers and sailors. These latter are kept under supervision for five days, and should be vaccinated against cholera.

Microbic Prophylaxis.—Efforts should be made to attack the infectious germ wherever it exists: in the patient, in the carrier, on soiled linen and underclothing, in privies, on the surface of the soil, in and about dwelling-houses, in polluted waters, on food, etc.

The microbic prophylaxis is accordingly extremely complex. Any negligence, or the omission to carry out any of the necessary precautions, will result in the spread of epidemic cases. The vibrio must therefore be followed, step by step, from the patient or the carrier, and we must seek to destroy it in each of the stages through which it passes, either in living or in inert media. *For this purpose the aid of the laboratory is absolutely indispensable to the rational prophylaxis of the disease.*

As soon as the threat of cholera exists, and, *a fortiori*, directly the first cases appear, special bacteriological laboratories should be mobilised for the examination of the first suspected cases. They should be amply equipped with the necessary appliances for collecting the dejecta of suspected patients, and with the appliances required for the cultivation and incubation and expert examination of cultures.

On the precise diagnosis of the first cases the fate of an epidemic will very often depend. The verification of the reactions of immunity in the blood of the persons affected is not so valuable as the discovery of the vibrio. It is of little use save as a means of retrospective diagnosis.

In the acute forms of cholera, above all when the rice-

like grains are observed, the cultivation of the stools in appropriate media readily yields cultures of the vibrio. This is not true, however, of ill-defined cases, or of slight diarrhœas ; it is therefore necessary to practise cultivations of the stools in these latter cases, as in the more authentic cases.

After death the autopsy and the bacteriological examinations should be made as promptly as possible. The vibrio is found in the exudate which covers the mucous membrane of the intestine, mingled with numerous epithelial cells.

It should be remembered that the cholera vibrio comprises a fairly large number of races, which differ in their dimensions—that is, in their length and thickness ; their form (some are rectilinear and rod-like, others ovoidal, almost like cocci) ; and their motility, which may even be lacking.

Cultivations should be made with one to five cubic centimetres of medium, and sometimes with much larger quantities, distributed in a certain number of receptacles containing 50 centigrammes of peptonised water. The examination should be made, at the latest, six to twelve hours later. Simultaneously cultures may be made in a mixture of agar and blood made alkaline with potassium. It must be remembered that *B. coli*, certain cocci, and *B. pyocyaneus* are also capable of multiplying on Dieudonné's agar. It is, in general, therefore, preferable to enrich the medium previously, rather than to commence the bacteriological analysis by cultivations made in peptonised water, before making discriminative cultivations on a solid medium.

The specific verification of the microbe isolated by agglutination *in vitro*, the test of injection into the peritoneum of an immunised guinea-pig, the indol reaction, and Bordet's reaction, will complete the investigation.

The permanent Committee of the International Bureau of Hygiene, in 1911, confided to M. Pottevin the

preparation of a report upon the bacteriological diagnosis of cholera. Italy, in 1915, published information of the same nature, indicating, at the same time, the means of removing and dispatching suspected matter. The latter (50 centigrammes) is placed in a glass receptacle, as are fragments of soiled linen. After death about six inches of that part of the ileum which lies immediately above the ileo-cæcal valve is removed, between ligatures. This material is enclosed in receptacles of thick glass, sterilised by boiling, and well stoppered.

Administrative dispositions and sanitary regulations have been adopted by European countries to prevent the introduction of cholera, and to combat its propagation and its sequelæ, during the present war. Sweden (Royal ordinance of the 9th of November 1915), Holland (the 15th of November 1915), etc., have decreed the precautions necessary to protect themselves against this disease, which has been prevalent among the Austrian, Turkish, and other troops, while it was imported into Italy by Austrian prisoners.

Consequently, a bacteriological diagnosis of the first case or cases should always be established. Without waiting for the result of the expert inquiry, all sick and suspected persons should be isolated, and such isolation should be extended to orderlies and nurses of either sex.

The case must be immediately notified by the physician, and access to such cases should be forbidden to any other persons than the physician.

Isolation premises should be sufficiently removed from other buildings, and must be provided with special closets and a special drainage system.

Nurses and orderlies should be vaccinated against the disease. The sick person's clothes and underclothes should be placed in a sack for disinfection and sent to the oven.

If disinfection cannot be effected immediately clothes should be plunged into a vat containing water to which

Javel's solution has been added, in such proportions that the mixture contains 0·5 centigrammes of chlorine per litre. Linen polluted by alvine evacuations and vomit must be the object of special precautions ; such materials must be handled with tongs or hands protected by rubber gloves. Boiling lye, or even boiling water merely, kills the cholera vibrio instantaneously.

Bedroom utensils, basins, slop-pails, spittoons, etc., are to be disinfected with sulphate of copper (10 per cent.), or with powdered chloride of lime, or Javel's solution, 1 in 50. The dejecta and the vomit of the patient should, if possible, be incinerated after being subjected to the action of the above-mentioned antiseptics. They must not be deposited in the neighbourhood of wells or water-courses, or in gardens, or on dung-heaps, etc., etc.

Floors, walls, etc., subject to contamination are disinfected with boiling water and washing soda.

The usual articles used by the patient—bowls, spoons, plates, metallic drinking-cups, etc.—should be placed in a wire basket and plunged into boiling water made alkaline with washing soda.

The patient should be kept scrupulously clean, and disinfected with a solution of cresol or dilute Javel's solution, his hands being frequently washed. Cholera cases should be placed in a special ward and tended by a special staff, the members of which have been vaccinated against cholera. Precise instructions as to avoiding contagion, as to washing the hands, wearing rubber gloves, and effecting frequent changes of blouses, etc., should be given. Pencils, pen-holders and pins must not be placed in the mouth, and no one must eat or smoke in the cholera ward, but in a separate apartment, after a change of protective clothing and disinfection of the hands.

In country districts the supervision of the patient and those about him, and the application of the above-mentioned measures of hygiene, are only too often imperfectly carried out. The dispersion of fæcal matter

over the soil, in back yards, farmyards, roads, gardens, dung-hills, etc., favours the diffusion of the vibrio. It is therefore necessary to leave physicians or qualified assistants in such localities, whose business it will be to ensure that these rules are observed.

The same measures of disinfection are to be applied, in times of epidemic, to the dejecta of any persons suffering from even light forms of diarrhœa.

The stools of patients who have recovered are dealt with in the same manner, as long as the appropriate cultivations reveal the vibrio in them.

Dead bodies should as quickly as possible be wrapped in sheets which are strongly impregnated with cresol, and should at once be placed in water-tight coffins with a large quantity of saw-dust impregnated with cresol.

All doubtful or uncertain cases must be subjected to bacteriological examinations of the stools.

Identical precautions should be taken in the case of ships carrying cholera patients, or suspected persons, or in the case of ships hailing from contaminated ports. The International Conferences of Constantinople, Vienna, and Paris have issued regulations as to the hygienic and administrative measures designed to protect ports of arrival, and to prevent the spread of cholera. To this end, when an epidemic threatens, lazarettos are established in the ports of arrival. The above-named conferences have decreed that passengers and crews should be inspected and placed in quarantine.

Pilgrimages to Mecca are prohibited. Lazarettos are established in Egypt to stop travellers and provide the sick with attention. Similar measures are taken on the frontier and at the railway stations at which travellers coming from contaminated countries arrive.

It should be remarked that the above measures relative to the protection of frontier ports and stations, although of the greatest service, are not nowadays regarded as indispensable. We cannot guard absolutely against cholera by closing the frontiers. Healthy germ-

carriers, convalescents, and the water of rivers may effect the spread of the disease. So may imported food-stuffs.

Accordingly the quarantine system has been replaced in the principal ports by the careful medical inspection of passengers, and their medical and administrative supervision in whatever localities they go to. International prophylaxis has everywhere adopted very similar precautions.

In France the notification of cholera is compulsory. A decree of the 28th of August 1909 requires that a general sanitary supervision shall be exercised in respect of every traveller, package, or other object coming from a contaminated region. Sufferers from cholera are detained in a special hospital. Suspected persons are isolated for a period which must not exceed five days. The other travellers receive a sanitary passport, which they must present to the mayor of the commune within twenty-four hours of their arrival. They are then subjected to a special sanitary supervision for five days, and are visited in their place of domicile, and, if they are found to be infected, or regarded as suspect, they are immediately isolated. In Paris they must notify any change of address to the prefecture of police or the mayor of their arrondissement. All their luggage is officially disinfected. The importation of soiled linen, clothing, soiled bedding, rags, fruits, and vegetables is prohibited.

It is to be noted that these precautions do not take into account the possibility of contagion due to the carriers of germs, and the danger which these constitute. On the other hand, the period of five days allowed for medical supervision is assuredly too short when it is not completed, as is usually the case, by a bacteriological examination of the dejecta. *The incubation period of cholera may, as a matter of fact, exceed five days.*

To the above-mentioned precautions it is as well to add the special supervision of vagrants, nomads, pedlars, and itinerants. As regards inland navigation, the same medical supervision should be exercised in respect of boatmen, bargees, etc.

During epidemics, fairs, public meetings, etc., should be prohibited, as these multiply or prolong the causes of interhuman contagion. Lastly, *the practice of vaccination against cholera, on as extensive a scale as possible, should be urgently recommended.*

MacLaughlin, in order to facilitate the search for the cholera vibrio in the case of travellers arriving from countries where cholera is suspected, has recommended that they should be dosed with sulphate of magnesia, in the morning, on an empty stomach ; with the exception of children and persons suffering from diarrhœa. Under these conditions he made 2000 examinations in Boston and Providence. This procedure is said to be preferable to the removal of matter from the rectum by means of a plug of cotton wool. The administration of a saline purgative causes the reappearance of the vibrio in the excreta of convalescents or healthy carriers.

. . . . . .

The prophylaxis relating to contagion by means of intermediate agents, living or inanimate (indirect contagion), deals more particularly with articles of food, drinking-water, flies, clothing, underclothing, linen, the soil, and, generally, anything that may have been contaminated by the fæcal matter of cholera patients or germ-carriers, and anything that may have been employed as a receptacle of such fæcal matter.

Everything that may cause indigestion or diarrhœa, or may introduce the cholera vibrio, must be avoided : green fruits, cucumbers, oysters, shell-fish, high meat or game, etc. The use of purgatives is dangerous.

In times of epidemic cooked foods should be consumed—that is, foods disinfected by heat—while those foods which will not bear cooking (cheese, etc.) should be effectually protected from contamination by flies, which is sometimes difficult, and from germ-carriers, which is still more difficult. The employment of safes, dish-covers of wire gauze, napkins, etc., and the mechanical prophylaxis of kitchens, dining-rooms, mess-rooms, hospital wards, etc., against the access of flies,

by means of the fitting of screens of wire gauze or mosquito-netting in doors and windows, will prove of the greatest service.

The disinfection of latrines, privies and their approaches, by means of chloride of lime, protects them from the vibrios and the flies which distribute them.

Flies may be destroyed by means of fly-traps, fly-papers, and powdered pyrethrum, scattered at night over shelves and tables, and by means of saucers containing a little beer, to which a fiftieth part of formalin has been added.

It is needless to insist that in times of epidemic it is necessary to drink no water that has not been carefully purified. Sterilisation by boiling constitutes a perfect guarantee of safety. Extremely susceptible to antiseptics, the cholera vibrio is killed in a few minutes by chlorine, in the proportion of 1 milligramme to 1 litre of water. Hence the value of sterilisation by means of Javel's solution, or the special tabloids of hypochlorite of calcium (Vincent and Gaillard). The Lambert process also affords an excellent means of destroying the cholera vibrio.

The prophylaxis of cholera in barracks, camps, and cantonments, and, lastly, among troops in the field, calls for the same general measures as those which have just been indicated. In time of war, it cannot be denied that this prophylaxis would offer considerable practical difficulties were it not that specific vaccination against cholera affords a real, though not an absolutely complete, protection.

An early diagnosis must be made of every case of cholera, and, without waiting for results, the patient or suspected person should immediately be isolated, and the premises or quarters involved, together with the latrines, should be immediately disinfected. All benign cases must be made the object of bacteriological examination, and patients must not leave hospital until two bacteriological examinations of the stools have been made, at an interval of a week.

Ambulance cars should be disinfected (with boiling water and washing soda or Javel's solution, the stretchers and canvas, etc., being washed).

The bacteriological laboratories should also undertake the bacteriological analysis of water supplies.

In France, in time of peace, a special delegate, appointed by the Prefect and approved by the Minister of the Interior, is instructed to place himself in communication with the chief officers of the Army Medical Service in the fortresses, hospitals and infirmaries, with a view to taking all prophylactic measures in the interests both of the army and the civil population.

Public water-closets, whether free or otherwise, should be inspected and disinfected. Urban disinfecting stations should be created, while disinfecting appliances and automobile ovens should be placed at the disposal of small towns and country districts.

A public notice might usefully be posted up, indicating the principal ways in which cholera is propagated, the part played by the dejecta of cholera patients and of certain healthy subjects, the part played by water (insisting on the point that it is not the only agent of transmission), and the necessity of notifying the medical or sanitary authorities in cases of suspicious illness, etc. The deposition of fæcal matter in farmyards, stables, manure-pits, roads, and lanes must be forbidden. The exportation of clothing, linen, rags, etc., from districts in which cholera is prevalent should also be prohibited, unless these articles have been subjected to disinfection by steam under pressure.

Specific Prophylaxis : Vaccination against Cholera.— Vaccination against cholera constitutes at the present time a really efficacious method of protection against the disease. It was first practised in 1885, by Ferran, in Spain. This physician discovered that guinea-pigs which had escaped death from infection due to the vibrio were protected against a deadly dose of virus. He cultivated the vibrio in bouillon at a temperature of 37° C. and injected living cultures of the microbe.

Haffkine inoculated the vibrio into the peritoneum of the guinea-pig, and, after passing it through several animals, which increased its virulence, he cultivated it in bouillon, in large, well-ventilated flasks, in which it became attenuated. It was this culture which he inoculated as vaccine.

Vaccine sterilised by heating to 56° or 60° C. (130° or 140° F.) has been employed in Russia, Germany, Greece, Italy, Serbia, etc.

Besredka has recommended an anti-cholera vaccine sensitised by the same method as that which he employed for anti-typhoid vaccine.

Vincent has prepared and employed, in France, Serbia, etc., an anti-cholera vaccine sterilised by ether. This vaccine is prepared with five races of vibrios, derived, as far as possible, from the countries in which cholera is prevalent. The vibrio is killed in less than one minute by the action of ether.

These vaccines afford experimental protection against the subcutaneous, or even intra-peritoneal, injection of extremely virulent vibrios.

In man the injection of Ferran's anti-cholera vaccine, which necessitates one or two repetitions of the injection, produces an intense local reaction (pain, œdema, redness, fever), and a general reaction (fever, etc.), and sometimes diarrhœa, lasting one to three days.

Haffkine injected under the skin of the flank $\frac{1}{10}$ or $\frac{1}{20}$ of an attenuated culture made on agar. Three to eight days later he injected the same dose of fixed and exalted virus. Later Haffkine employed the latter exclusively.

Powel inoculates in one injection $\frac{1}{6}$ of a culture on agar of Haffkine's exalted virus. Sterilisation by heat and antiseptics (carbolic acid), "without destroying the vaccinating property of the Haffkine vaccines, diminishes it considerably" (Salimbeni).

Between April and October, 1885, Ferran administered 150,000 preventive inoculations to 50,000 people.

With remarkable patience and perseverance, Haffkine, between April, 1893, and September, 1895, vaccinated 42,197 persons by means of nearly 70,000 injections. The vaccine was living. The number of subjects vaccinated by his method has been considerably increased since then. The vaccinations have been carefully checked, and their results compared with the morbidity of persons subjected to similar conditions of infection. In each locality one-half only of the inhabitants were vaccinated, the other half serving as a control. The results testified to an efficacy which was not absolute, but was genuinely considerable. The immunity, it was said, might continue for twelve to fourteen months.

Aldo Castellani, in 1909, adopted the employment of living cultures as vaccine, a method which Ch. Nicolle has also employed. For the first injection he recommends Wright's dead vaccine.

The employment of vaccine sterilised by heating has been recommended in Germany. Two milligrammes of a culture made on agar (a platinum loopful) is injected, diluted with physiological water, and with the addition of carbolic acid. The injection is accompanied by considerable local and general reaction.

For four days there is said to be a negative phase, with predisposition to infection (Testi).

Cawadias has stated that during the epidemic which broke out in the Greek Army at the time of the last Balkan War, his cholera patients included :

82·5 per cent.		of non-vaccinated subjects
10·6	,,	of incompletely vaccinated subjects
6·7	,,	of completely vaccinated subjects.

Among the non-vaccinated there were 21 per cent. of deaths ; among the vaccinated patients, 2 per cent.

Arnaud has published similar data.

In Russia an official circular appearing in 1909 recommended vaccination against cholera.

Three injections were made, the first consisting of 0·5 to 1 c.c.; the others of 2 and 3 c.c. One should avoid vaccinating persons suffering from cholera, persons suffering from febrile complaints, and weak or anæmic persons.

About this time Zverev collected and classified the observations of a large number of hospitals: 28,996 persons were given preventive injections. The number of injections was only 53,162. The reaction caused by the injection was slight in 58 per cent. of these, of medium intensity in 32 per cent. (involving lassitude, vertigo, severe headache, nausea, colic, diarrhœa), and severe in 10 per cent. (involving violent headache, vomiting, frequent diarrhœa, pain, high fever, and incapacity to work for several days).

As regards the immunising effects, only twelve persons contracted cholera. In addition to these, twelve persons fell ill one to three days only after vaccination; the injections, therefore, had no abortive action on the cholera.

Two suffered from diarrhœa of a choleraic type, 12 and 15 days after an injection, and rapidly recovered. One nurse had cholera 2 months and 5 days after the second injection, and recovered. A woman of forty-four developed cholera 30 days after the second injection, and died.

The immunity conferred by vaccination has in general been high.

Kasch Kadarrov has published an essay giving particulars of the vaccination of 16,011 persons by means of 30,078 injections. Of these persons 6352 received one injection (that is, 39·7 per cent.); 5251 received two injections (32·8 per cent.); and 4408 received three injections (27·5 per cent.).

34·6 of those vaccinated suffered reactions: severe in 13·5 per cent., of medium intensity in 32·4 per cent., and slight in 54·1 per cent.

The fact of immunity was thoroughly established,

but only several days after the injections. The duration of the immunity was brief (a few months).

It is estimated that the duration of the immunity conferred by vaccine sterilised by heating is not in general more than six months.

Aaser, of Christiania, made an anti-cholera vaccine (by heating) with a very virulent race of vibrios, and vaccinated thirty-one persons, nearly all of whom exhibited local and general reactions.

In the Val-de-Grace laboratory an anti-cholera vaccine is prepared with ether. This vaccine is polyvalent—that is, it is prepared with five races of vibrio, obtained from countries actually infected (Galicia, India, etc.). This vaccine has been injected into several thousands of soldiers in France, Serbia, etc., and gives rise to no local or general reaction. It causes neither swelling, nor pain, nor fever, and may be injected, as it is so readily tolerated, into any individual, without any counter-indication save incipient cholera. Two injections are given at five days' interval: one of 2 c.c. and the other of 2·5 c.c.

The Serbian troops were vaccinated by means of two vaccines, one prepared by means of heating and one with ether. The result was an excellent degree of protection.

The same vaccines were employed in the Italian Army, cholera having been imported by the Austrian prisoners; but the disease was very quickly suppressed.

In the German Army vaccination against cholera has been practised systematically beginning a few months after the commencement of the war.

We possess certain data as to the vaccination of the Austrian troops in Cracow, where cholera was prevalent. The mortality among the non-vaccinated was 50 per cent.; among the vaccinated, 6·5 per cent. The vaccinated subjects developed a fairly large number of slight forms of cholera. Vaccination effected during incubation or even in the initial stage of cholera does not appear to have produced any evil effects.

Moreschi and Marcora have recommended intravenous vaccination, in preference to subcutaneous vaccination. The dose injected is 0·1 to 0·3 of an ordinary platinum loopful, instead of six loopfuls (nine milliards of vibrios) injected under the skin.

PART I.—CLINICAL SURVEY

CHAPTER XV

SYMPTOMATOLOGY

Typhus,[1] an acute infectious malady, without special anatomo-pathological lesions, the specific agent of which is not yet known, is characterised by a continuous fever, lasting, on an average, a fortnight, and by morbid symptoms which are chiefly nervous and respiratory. One of its symptoms, and the most constant, is the appearance, during the first days of the disease, of a characteristic exanthem.

The clinical development of typhus consists of four periods :

1. The period of incubation.
2. The period of invasion.
3. The period of eruption.
4. The period of termination.

1. **Period of Incubation.**—The duration of the period of incubation varies from 5 to 21 days. According to Jeanneret-Minkine it averages 8 days ; according to V. Bué, 10 days ; according to A. Netter, 11 days. Marsh and Netter have reported cases where invasion followed almost immediately upon infection. In general, this period is not marked by any indication which particularly draws attention to it. Toward the end, however, one may note certain digestive disorders (a condition of nausea and anorexia), headache, lassitude and vertigo, while the disposition of the

[1] Synonyms : *Exanthematic typhus, typhus petechialis,* "spotted typhus," "camp typhus," etc.

patient seems changed. The temperature is 99·5° F.; the pulse eighty beats to the minute. On the following day the headache is more violent, the anorexia more complete. The temperature rises to 100·2°. The patient already wears a jaded expression, which bears no relation at all to his condition. He complains, often enough, of sharp pains in the limbs, pains in the spine, headache, and vertigo, with buzzing or humming in the ears, during the days which immediately precede the first appearance of the symptoms.

2. **The Period of Invasion.**—Sometimes after two or three days of these prodromes, but oftener quite suddenly, the patient is attacked by a violent and peculiar fit of shivering, an excruciating headache, frequent vomiting, and epistaxis, the persistence and profusion of which alarm those who witness it, sometimes necessitating plugging (Bué). The temperature rises to 102°, and may reach 104° or 105°; the pulse is rapid, 100 to 120 beats per minute. The respiration is accelerated, and there is cough, with signs of slight bronchitis. *The face is congested and the conjunctivæ injected,* and a muco-purulent discharge is sometimes observed. The eyelids are tumefied. Sometimes, from the commencement, the patient is violently delirious. The tongue is coated. The pharynx is inclined to redness. The epigastric region is painful upon pressure, and the patient is usually constipated; the abdomen is not painful. Diarrhœa is not exceptional, however, and is accompanied by abdominal rumbling and pain provoked by pressure. Combemale has reported cases of choleriform diarrhœa. The urine, scanty, and dark in colour, contains albumin. The patient is apathetic. His sleep is disturbed, interrupted by dismal dreams; sometimes there is even complete insomnia, the patient being unable to obtain even ten or fifteen minutes' rest. Narcotics are generally powerless to afford relief (H. de Brun).

3. **The Period of Eruption.**—From the fourth or fifth

day (Netter, Jeanneret-Minkine, Escalier, etc.) the exanthem of typhus appears, an exanthem which is not, however, constant, and which may be lacking in one-tenth or one-twentieth of the cases observed (Netter). It commences on the trunk; it should be looked for first of all under the armpits, on the shoulders, then in the region of the epigastrium, and on the thorax; finally, on the limbs and the abdomen, where the eruptive elements are sometimes very numerous. The eruption presents two different aspects, which differ greatly. At certain points the patient's skin is sprinkled with marblings, due to the appearance, under the epidermis, of very fine, pale, irregular spots. But the eruption which occurs with by far the greater frequency consists of spots which present no relief, or very little, yet which are sometimes papular, with rounded but ill-defined contours. These spots are at first rose-coloured or reddish, but they afterwards assume a livid, bluish tint. Their size varies from that of a small pin's head to that of a large lentil. Often isolated, they may, however, be confluent, and their outlines then become irregular and indented.

On their appearance the spots disappear for the moment on pressure, like the rose-coloured, lenticular spots of typhoid, but two or three days later they are surrounded by a very pale bluish-grey halo. If they were raised they now subside. It seems as though the skin had suffered a slight contusion at this point: slight, but sufficient to produce a tiny patch of ecchymosis, *which no longer disappears under pressure.* This *petechial* aspect may not be presented by all the spots. With moderate frequency (in 10 per cent. only of the cases occurring in an epidemic observed by Jeanneret-Minkine during the present war), the spots undergo a hæmorrhagic transformation; they are then completely reminiscent of the spots of purpura. They are first observed in the region of the back and the tracts exposed to continuous pressure (Escalier). The typhus spots persist, on an average, for five to ten days. Most

of them disappear without leaving any traces, but others reveal their position, sometimes until the end of the convalescent period, by a bluish tinge or a slight pigmentation of the skin.

The eruption of typhus sometimes appears very early, and is also extremely fugitive. *It may be confined*, even in fatal cases, *to a few spots*, lightly marked, which sometimes have to be carefully sought for (H. Vincent). It may even be absent in children under fifteen years of age. The spots may become more visible, or assume their characteristic aspect, after washing the arm with soap, and then tying a ligature round the root of the limb. They should be sought on the palm of the hand, which, according to some writers, is their favourite situation.

Appearing simultaneously with the exanthem, or sometimes even earlier, there is an erythema characterised by a deep, diffuse redness of the mucous membranes of the mouth, invading the pillars of the soft palate, the uvula and the tonsils (Bué, Petrovich). From the second day, on the mucous membrane of the palate, a certain number of red spots (5 to 15), from 1 to 3 millimetres in diameter, may sometimes be observed. They very soon disappear. Their outlines are denticulated.

These buccal spots invade the respiratory passages. All sufferers present, from the outset, a dry, fitful cough, which later on is accompanied by expectoration. This is often very profuse, purulent, and fetid.

The appearance of the eruption coincides with an aggravation of the intensity of all the morbid symptoms. The nervous disorders and the delirium are aggravated. The eye is haggard, the face now pale, now flushed. The temperature oscillates between 104° and 106° ; the pulse is small and feeble ; the number of beats, in cases of average severity, being from 110 to 120 per minute. It is at this stage that sudden impulses toward suicide are observed, and extreme agitation, during which the patient seeks to get up and go out ; if he is not watched he will make his escape. In the benign forms

of the disease the nervous system is not greatly affected by the toxins; the sick physician will take notes of his own case (Bué). However, in addition to the spinal pains and gastralgia which are not uncommon, a cutaneous hyperesthesia may be observed, local or general, and sometimes extremely intense.

Toward the eighth day it seems as though the disease were about to reach its termination. The temperature falls a couple of degrees, or even four; but this deceptive remission is of brief duration (twenty-four hours at most). The fever reappears, as severe as before, and is maintained until the fifteenth day.

During this second portion of the critical period nervous disorders are constant, more or less accentuated, and varying infinitely in the case of different patients. Certain sufferers exhibit a calm and gentle delirium; plunged in a semi-torpor, they mutter incoherently. In others the delirium is definitely systematised, revolving round a fixed idea.

Lastly, a delirium of action may be observed, which is influenced by terrifying hallucinations. It is very similar to that of *delirium tremens* (de Brun), and is accompanied by a return of the suicidal impulses.

Convulsive crises have also been observed (R. Job and E. Ballet).

Generally speaking, the delirium is not of long duration, although in certain cases it has been known to persist even after defervescence (de Brun). Often enough it disappears after two or three days, to give rise to prostration and stupor. About the ninth day of the disease the patient is inert, lying in the dorsal decubitus, the eyes almost closed, the pupils contracted, the hearing much impaired. The patient is completely indifferent to all that is happening around him; he does not recognise those about him, and it is very difficult to rouse him from his torpor. Sometimes he is plunged into a sort of coma, which lasts until defervescence or death.

However slight it may be, the prostration of the

typhus patient is of a very special kind. Remlinger has recently drawn attention to one of its peculiarities, which he has called the "sign of the tongue." The typhus patient cannot protrude his tongue from his mouth, or can do so only at the cost of extreme effort. Fumey, Godelier, Billot, Maurin, Masse, and H. de Brun had already noted this fact, and also that in certain cases the tongue even seemed to be retracted toward the pharynx. Some writers, moreover, have noted fibrillary movements, and tremors of the tongue, as well as difficulty in speaking. In 1893, referring to the nervous manifestations which he had observed during the Beyrout epidemic, H. de Brun remarked: "The tongue seems as if fixed to the floor of the mouth; it is heavy and sticky, and is moved with difficulty; speech is slow and often tremulous. . . . When the tongue is protruded from the mouth it is animated by incessant vermicular movements; it is always moving, and cannot be kept motionless in one position; the commissures of the lips also are twitching, owing to the trembling of the levator muscles, and the whole jaw may jerk so violently that I have sometimes found it impossible to take the buccal temperature. In forms of medium or slight intensity the speech is conspicuously tremulous, and this symptom may persist so long after defervescence that it has enabled me to form a retrospective diagnosis six weeks after recovery."

Congested, broad, and more voluminous than in the normal condition, the tongue is covered with a mucous coating which is at first white, then yellow, then brown or black, thick, and covered with cracks. The edges and the tip are a bright red. At other times it is small, dry, and withered, as though baked and shrivelled. The lips and teeth are dry, black, and fuliginous.

Tremors are not localised only to the tongue, lips, and jaw; they may also be observed in the hands and forearms, the oscillations here resembling alcoholic tremor (de Brun).

Subsultus tendinum is more constant and more accentuated than in typhoid fever.

The cutaneous, abdominal, and cremasteric reflexes are fairly constantly suspended (Potel).

The abdomen is flat, or slightly distended; constipation is persistent, or else one or two diarrhœal stools may be observed. There is often relaxation of the sphincters, evacuation and urination being involuntary. Sometimes also there is an actual retention of urine which necessitates the use of the catheter.

The urine, rather more abundant than at the outset, very frequently contains albumin, with or without any increase of urea. The albuminuria noted in 50 per cent. of patients usually disappears about the fifteenth day. The skin is hot, sometimes moist. The pulse rarely exceeds 115 to the minute; it is small, feeble, compressible, and often intermittent (Netter). The spleen is slightly enlarged. The emaciation is extreme. The vaso-motor sign of supra-renal insufficiency is pretty constantly observed (Bué). Combemale in four cases has noted a development on the face, of a greyish, crystalline efflorescence; two of these cases died in a few hours.

4. **The Period of Termination.**—Death occurs in 15 to 50 per cent. of the cases, the period of its occurrence varying; but it most frequently supervenes during the second week, on the eleventh, twelfth, or thirteenth day (Jeanneret-Minkine). It is most commonly due to a sudden cardiac syncope.

In favourable cases a critical improvement occurs on the fourteenth or fifteenth day. Very rarely defervescence is sudden, occurring in a few hours. More commonly the temperature falls slowly, defervescence assuming the form of lysis. In three, four, or five days it becomes normal, or even subnormal. At the same time the pulse suddenly falls to 80, and is sometimes even abnormally slow, while maintaining the normal qualities of rhythm and tension.

The skin scales off in fine, small, squamous flakes, which, as they approach desquamation, give the skin a greyish-white, metallic lustre (Escalier). The nervous symptoms are progressively abated, and in a few days have disappeared. Sometimes, after a peaceful sleep, of several hours, the patient awakes transformed. He recognises those about him; he is no longer delirious, but his deafness usually remains and is more or less marked, while the haggard expression persists for some weeks.

The tongue grows moist and clean; the appetite returns and is insatiable; there is frequently a sudoral, polyuric, or diarrhœal crisis.

Muscular impotence is very marked, and emaciation extreme. *The convalescence is always long*, the strength returning slowly, and the patient is very quickly fatigued. For about a month the convalescent experiences a sensation of physical depression and general exhaustion, an exaggerated need of food and very prolonged sleep.

Recurrence is rare, but possible.

Complications

The complications which may make their appearance during convalescence are numerous.

Among these we must give the first place to *myocarditis*, which is, if not of invariable occurrence, yet extremely frequent, and is betrayed by the acceleration and enfeeblement of the cardiac pulsations, the very marked deadening of the heart sounds, the diminution of arterial pressure, and the failure and irregularity of the pulse. A careful examination of the heart should be made every day, in order to provide against the sometimes fatal complications which accompany cardiac insufficiency.

Broncho-pulmonary complications are also frequent. *Simple bronchitis*, *capillary bronchitis*, *pneumonia*, or *broncho-pneumonia* may be encountered. The patient may complain neither of a stitch in the side, nor of

a cough, nor of expectoration; but only show an acceleration of the respiratory movements, with a slightly purplish, cyanosed coloration of the face. *Vomicæ* have been recorded (Combemale), *pulmonary gangrene*, and *purulent pleurisy*.

Laryngo-typhus may be observed, as well as *ulcerations of the vocal cords*, and *laryngeal perichondritis* with *œdema of the glottis*.

Sacral, *trochanteric* and *malleolar* bed-sores are not uncommon.

Gangrene of the mouth, the scrotum, the *labium majus*, the extremities, and the lower limbs, principally through arterial obliteration, is fairly common; it may vary considerably in extent, sometimes necessitating numerous operations.

Periostitis and *peripheral neuritis* (Job and Ballet, Bué) are also observed with some frequency, as are *lymphatic suppurations*, *phlegmons*, *adenitis*, and *erysipelas* (Delearde and d'Halluin), etc.

Suppurative otitis media and *suppurative parotitis* are frequently observed, as is also *phlegmasia alba dolens*. Certain patients suffer from a considerable œdema of the lower limbs long after recovery from typhus, and this sometimes coincides with œdema of the eyelids, most frequently without albuminuria. Lastly, Delearde and d'Halluin and Bué have noted the exceptional gravity of *bucco-pharyngeal diphtheria* when it develops during the developing period of typhus, or during convalescence, and the frequency of various *tubercular* manifestations which may sooner or later appear.

Clinical Forms

A certain number of clinical forms of typhus have been described, which are differentiated by the predominance of certain symptoms, or the rapidity with which the disease develops. We shall briefly recapitulate these forms.

Inflammatory Typhus.—A form which occurs in young and vigorous subjects, and persons belonging to the wealthier classes; it is characterised by a high temperature, violent headache, and acute delirium, in the course of which attempts at suicide are not uncommon.

Ataxic Typhus, Adynamic and Ataxo-Adynamic Typhus.—These forms are sufficiently characterised by the symptoms which serve to indicate them; they are usually serious.

Typhus siderans (Jaccoud), in which death may ensue in two or three days, sometimes in a few hours. This form is observed in alcoholics (Baudens).

A *slight form of typhus*, of very brief duration, is also described by Hildebrand as *typhus levissimus*; it is not accompanied by eruptions. In this case the initial period may pass unperceived unless it was known that an epidemic of typhus existed. It is generally sudden, with shivering, headache, vertigo, lassitude, and insomnia. The tongue is coated, the skin hot, the spleen slightly enlarged, and a little bronchitis may be present. These symptoms increase for four or five days; then the disease quickly terminates. The patient breaks into profuse sweats, and frequently exhibits labial herpes. These cases have been described by Netter as *ephemeral fever*. There are also abortive forms, with violent onset, which suddenly abate after three or four days. The patient frequently suffers from facial herpes.

Lastly, Jacquot has described a series of symptoms: malaise, slight fever, loss of appetite, nausea, headache, and intellectual debility, which may be exhibited for several weeks by subjects exposed to contagion, but who, apparently, have not contracted typhus. Jacquot describes this condition as "*typhisation in small doses.*" Combemale noted similar clinical phenomena during the Lille epidemic. They are due to attenuated forms of the infection.

CHAPTER XVI

DIAGNOSIS

At the beginning of an epidemic, or when isolated cases of typhus are occurring, the diagnosis is not easy. It is always uncertain before the appearance of the eruption (Murchison).

The sudden onset, the high temperature, rising to 104° or 105°, the rapid pulse, of 100 to 120 per minute from the first days of the disease, the early appearance of the nervous symptoms (on the second or third day), the presence of constipation without intestinal phenomena, the profuse and frequent epistaxis, the phenomena of congestion, the injection of the conjunctivæ, the state of the mucous membranes, and upper air passages, and the almost constant vomiting are assuredly not to be disdained as elements of diagnosis. They do not, however, acquire their full validity until the appearance of the exanthem, with all its characteristics: its sudden commencement (on the second to the fifth day), its petechial character, the abundance and the general distribution (except on the face) of the eruptive elements, and the successive transformation of these elements, which persist for some length of time. Lastly, the verification of the exanthem, the "sign of the tongue," the nervous phenomena, and, above all, the tremor and the loss of memory are very diagnostic.

The physician, in pursuance of Netter's advice, may derive great assistance from the following factors:

1. The existence of transmitted cases among the members of the medical staff (physicians, orderlies, nurses, etc.).

2. The social position of the first sufferers (vagrants, destitute persons, prisoners, etc.).

3. The not infrequently advanced age of the patients.

4. The predominance of the disease in cold weather.

The diagnosis is usually facilitated by such factors as the knowledge that an epidemic exists; the well-established fact that the patient comes from a house where there have been cases of typhus; that he has been in direct or indirect contact with persons suffering from typhus. But even in such cases as this it is necessary to establish a precise differential diagnosis.

Typhoid fever is, of all diseases, the one which presents the closest clinical analogies to typhus. Here, however, the commencement is usually much less sudden; the injection of the conjunctivæ, so peculiar to typhus, is absent in typhoid fever. The eruption appears later, and is less abundant. However, the rose-coloured spots may become generalised, may attain large dimensions and, especially in time of war, may be purpuric or hæmorrhagic in character. In typhoid fever diarrhœa is more frequent than constipation; in typhus the converse is true. In typhus the temperature rises to 104° or 105° at the outset, and remains at that level for five or six days, without any notable remission. During the present war the general signs and symptoms of torpor have sometimes been so marked during the course of typhoid fever and paratyphoid fever that one might have believed them cases of typhus. In such cases the sero-diagnosis of non-vaccinated subjects, or the cultivation of the blood, during life, and of the bile, after death, make it possible to establish a diagnosis. In Serbia, during the present war, Petrovich observed instances in which typhus made its appearance in typhoid wards. On the second day the patients exhibited photophobia and turgescence of the face, while a dark, diffuse redness, with roseate spots, covered the throat; the tongue was coated and was red at the edges and the tip. On washing the arms and the trunk with soap it was possible to verify the

commencement of the exanthem. The heart sounds were already weakened.

Relapsing fever begins in a much more sudden and dramatic manner than typhus ; there is violent shivering, nausea, bilious vomiting, a temperature of 104°, 106°, or even 107°, and more from the outset ; there is enlargement of liver and spleen, the latter being painful upon percussion. These phenomena suddenly disappear at the end of four, five or six days. The temperature falls to normal and the patient may think he has recovered. But after the lapse of about a week a fresh attack develops, in every way resembling the first. There is no exanthem, or at most a limited roseola may be observed, but this is exceptional. Moreover, during the whole course of the attack an examination of the blood reveals the specific spirochæte.

Malarial fever of the continuous type is not usually observed during the same season as typhus in countries where malaria and typhus are endemic. Typhus is more common in the winter and spring, malarial fever in the summer and autumn. The hypertrophy and the consistency of the spleen, the absence of an exanthem, and stupor, combined with the knowledge that malaria is prevalent, and finally, the examination of the blood, and the discovery of the malarial parasite, will establish the diagnosis, and the efficacy of treatment by quinine will subsequently confirm this.

The eruption of typhus has caused the disease to be confused with measles, especially in children. The prodromic period of measles is highly characteristic, with its coryza, its epiphora, and its sneezing. The eruption, which appears about the fourth day, involves the face, which typhus respects. In measles the temperature falls as soon as the exanthem appears ; the spleen is normal.

Cerebro-spinal meningitis has also been confused with typhus. In meningitis there is photophobia, and a dread of noise, while in the typhus patient there is usually deafness, and the senses are dulled. The face

of the sufferer from meningitis expresses suffering and anxiety; that of the typhus patient stupor and indifference. In meningitis there is stiffness of the nape of the neck, and Kernig's sign is present; there is no exanthem.[1]

Influenza may give rise to exanthemata like that of scarlatina, or measles, or papular eruptions (Van Swieten, Comby, Perrenot), with redness of the pharynx and a typhoid aspect, which may give rise to confusion at the beginning of epidemics. The onset of influenza is even more sudden than the onset of the sudden form of typhus. The temperature, which at first rises to 104° or 106°, remains only for a short time at that level. Sometimes it drops suddenly, after two or three days, and does not again rise; sometimes, after a sudden and very marked fall, lasting twelve to twenty-four hours, it rises as high as before the fall, forming a depression in the thermal curve like an inverted steeple (J. Teissier's "V of influenza"); sometimes it falls by lysis. Apart from the behaviour of the temperature, the oculo-nasal catarrh, the arthralgia, the neuralgic character of the headache, which is often supra-orbital, and the frequent perspirations, will enable the physician to form a diagnosis.

Apical pneumonia is sometimes accompanied by typhoid-like phenomena, though, for several days, despite careful examination, it may be impossible to discover local indications. The commencement is, as a rule, easily specified; the dyspnœa, the dryness of the tongue, the redness of the cheek-bones, the presence of herpetic vesicles, the absence of petechiæ, and, lastly, the examination of the lungs, will assist the physician to establish his diagnosis.

The spotted fever of the Rocky Mountains presents remarkable points of resemblance to typhus: it commences with violent shivering; the temperature rises to 104° or 106° by the second day, and between the

[1] In certain cases purpuric spots appear in cerebro-spinal fever, whence the name spotted fever.—Ed.

second and fifth days an eruption appears, exactly like that of typhus; rose-coloured spots which become generalised and are transformed into petechiæ, but which first appear on the wrists and ankles; not until later do they reach the thorax and the abdomen. Moreover, there is constipation, enlargement of the spleen, delirium, a sub-icteric tinge of the skin and the conjunctivæ, scanty and albuminous urine and œdema. This disease prevails more particularly in spring and summer. Wilson and Chowning claimed that it was due to a piroplasma, which was rare in the peripheral circulation, but, on the other hand, abundant in the visceral circulation. Their discovery has not been confirmed by the researches of Stiles and Ricketts.[1] Quinine in large doses is said to possess a curative action in Rocky Mountain spotted fever (Anderson).

Finally, it must be remembered that there are cases in which diagnosis is rendered extraordinarily difficult by the association and overlapping of two quite different maladies, these giving a type of "mixed malady" (Kelsch, Remlinger), which does not in any way resemble either of them. Among these mixed maladies we should specially mention the association of typhus with recurrent fever, with typhoid fever, with dysentery, and with scurvy. Exceptional in time of peace, these morbid associations are not rare in time of war. It is important to be forewarned of their existence.

[1] It is now generally accepted that Rocky Mountain spotted fever is a variety of typhus. The disease is spread by ticks.—Ed.

CHAPTER XVII

TREATMENT

A PATIENT definitely attacked by typhus, or merely suspected of typhus, should immediately be isolated in a spacious, well-ventilated room. Bodily cleanliness should be scrupulously attended to. Diet should consist of liquids : milk, beef-tea, lemonade, with the addition of wine, and diuretic beverages in abundance. Alcoholic drinks and preparations should be reserved for patients whose hearts are weak. The very numerous systems of treatment which have been recommended have not always given the excellent results which were expected of them. Among these we may refer to the blood-letting treatment (Clutterbuck and Armstrong), the stimulant treatment (Alison, Graves and Stockes), the hydrotherapic treatment (Currie), the quinine treatment (Dundas), the emetic treatment (Rasori), etc.

The best treatment is the symptomatic one. High temperatures and intense cerebral phenomena are beneficially influenced by lotions (Petrovski), and warm, or, better, cold baths.

The headache which is so troublesome during the first few days may be combated with preparations containing opium, with aspirin, or with cryogenin. The latter, according to Marini (of Aleppo), has the further advantage, in cases of typhus, of lowering the temperature, regulating the pulse, and procuring for the sufferer a sort of euphoria.

Constipation, if it is present, should be treated by emollient or slightly purgative enemas, or by laxatives. No attempt is to be made to establish diarrhœa. The

respiratory organs, the heart, and the urinary secretion must be closely watched, and complications treated by the usual means. In cases of cardiac collapse during typhus, Jeanneret-Minkine recommends massive injections of ethero-camphorated oil.

Bouyges claims to have obtained good results by intravenous injections of electrargol and colloidal gold. This last drug excites powerful reactions, and must not be employed when there is myocarditis.

Gaston has reported good results from intravenous injections of citrated and iodised serum.

Legrain and Raynaud (Algiers) have treated typhus patients by subcutaneous injections of the serum of convalescents. The temperature has fallen very quickly, has remained low for thirty to thirty-five hours, the pulse has improved, the general condition has been ameliorated, and the patients have recovered.

During the present war Escluse and Liber have attempted to treat typhus by means of intravenous injections of the blood of convalescents, coagulation being retarded by citrate of sodium. By this method they claim to have obtained recoveries in cases which were despaired of. The injections should be made from the fourth to the tenth day at latest. The blood should be drawn from a robust convalescent whose defervescence dates back only eight or ten days. Thirty c.c. may be injected with impunity during the twenty-four hours, in three instalments. The recovery of the patient may depend upon perseverance in the treatment.

Finally, Charles Nicolle and Ludovic Blaizot have been able to produce a condition of hyper-immunisation in the ass and the horse, by administering repeated inoculations of emulsions of the spleen or supra-renal capsules of guinea-pigs infected with typhus. The serum of these animals is said to possess actual preventive power, and an undeniable curative power. Non-toxic to man, it has been administered in thirty-eight cases, and thirty-seven times with success.

MM. Nicolle and Blaizot give the treatment as follows :—

1. There is much to be gained by commencing the serotherapeutic treatment at the very commencement of the disease, immediately the diagnosis is admitted, or even suspected merely.

2. The inoculations should be repeated daily until defervescence, or, at all events, until a real and profound improvement of the general condition is obtained, foreshadowing an imminent convalescence.

3. The proper doses of the serum are 10 c.c. to 20 c.c. daily, administered hypodermically.

4. The serotherapeutic treatment should be completed by a medical treatment designed to favour the elimination of the microbic toxins and the residues of the defensive reaction of the organism. This medical treatment consists of abundant diuretic beverages, tepid baths (82° to 90°), stimulants, and cardiac tonics ; lastly, in serious cases in which the intoxication is profound, it may be needful to inject 500 to 800 grammes of artificial serum.

PART II.—EPIDEMIOLOGY AND PROPHYLAXIS OF TYPHUS

CHAPTER XVIII

MEDICAL HISTORY AND GEOGRAPHY

Typhus is probably as old as man himself. We find descriptions which answer to this disease in the Hebrew scriptures and in the medical works of the Arabs. In the narrative of the terrible plague which ravaged Greece, and of which Thucydides was the historian, one recognises typhus. The first study of this terrible malady is due to Frascator. There was no lack of material for observation, for Italy was decimated by typhus between 1505 and 1530. Lautrec's army, infested by the disease, left 30,000 dead before Naples.

Since then there has not been a single war unaccompanied by typhus. Physicians learned to distinguish typhus (*Pesticula*), or *Typhus petechialis*, from plague, which was then common. All the wars of the sixteenth, seventeenth, and eighteenth centuries were, without exception, the occasions of a return of typhus. The armies of Charles V., before Metz, were ravaged by this disease. During the wars of the Revolution it was constantly active. The French, besieging the Austrians before Mantua in 1806, were as severely visited as the latter, and carried the germ back to France with them. At the same period 14,000 deaths were reported in Genoa. In France Montpellier, Marseilles, Toulon and Grenoble were infested by typhus.

After the battles of Austerlitz and Jena the

ambulances and hospitals were encumbered with typhus patients. The German prisoners brought the sickness to France. During the retreat from Russia the unhappy French troops, exhausted and covered with rags, died by the thousand along the road-side at Wilna. In the latter city, where 30,000 men had taken refuge, 25,000 succumbed; 8000 of the inhabitants also perished by typhus, the poorer inhabitants being principally affected. In Dantzig 36,000 Frenchmen were besieged; 13,000 died of typhus. There were 10,000 deaths among the civil population. At Torgau 14,000 men out of 26,000 succumbed. At Mayence also 20,000 soldiers died of typhus.

These frightful hecatombs amply justify the name which at this period was given to the disease—"army typhus," "camp typhus." It seems probable that typhoid, which presents clinical analogies to typhus, and which is the peculiar scourge of armies in the field, has shared with true typhus the responsibility for these terrible onslaughts.

Although typhus has not again broken out with such terrible violence, it has not, however, entirely disappeared.

After 1815 typhus persisted in convict establishments, hulks, and prisons, and also amid the poor and wretched populations of certain countries. It persisted in the East, in Russia, Prussia, Poland, Silesia, and Ireland. Between 1846 and 1848, according to Murchison, there were 300,000 deaths from typhus in Ireland. The Crimean War reawakened it. At first a few cases appeared among the Russians; then it spread rapidly; 12,000 cases and 6000 deaths were reported to have occurred in their ranks. The French Army was attacked in turn. The soldiers, crowded together in dug-outs and the trenches, exhausted, subjected to superhuman exertions, and deprived of the most elementary hygienic attention, were struck down in the proportion of one in ten (F. Jacquot). More than 17,000 succumbed. On their return the

armies infected the populations of Marseilles, Toulon, Porquerolles, and Avignon.

It is said that there were a few cases of typhus in the French Army in 1870, after the battle of Mans, and at Mayenne (Morisset), but this fact is not satisfactorily proved.

On the other hand, during the Balkan War the Army of the Danube had 32,451 cases (54·8 per 1000), and 10,031 deaths (17·02 per 1000). The Army of the Caucasus had 15,660 cases, with 6506 deaths.

The disease showed a few cases at the outset of the war, then spread rapidly, especially when the cold weather set in and the men were packed together in cattle-sheds.

The proportion of cases in the Army of the Caucasus was as follows :—

November, 1877	4·69 per 1000
December ,,	19·65 ,, ,,
January, 1878	43·85 ,, ,,
February ,,	46·90 ,, ,,
March ,,	38·13 ,, ,,
April ,,	22·65 ,, ,,
May ,,	12·38 ,, ,,
June ,,	6·08 ,, ,,

Erzeroum and Khorassan were the centres most severely infected. Certain regiments were almost annihilated. A company of the 74th Regiment, on entering Kara-Kilisse, was made up thus: First came a lieutenant, on a stretcher, paralytic, with sores. Beside him came his sub-lieutenant. These two officers, and eight men carrying the stretchers, represented all that was left of the company. "The rest," said Koslov laconically, "were in the hospitals or the tomb."

Typhus was again encountered by the belligerent armies during the Balkan Campaign of 1912.

There was no outbreak of typhus during the Manchurian War.

During the present war against Germany no case of typhus has so far been observed in the French Army.

Bacteriological investigations have shown, in certain suspected cases, that these were really malignant and hypertoxic forms of typhoid fever, the typhoid bacillus being isolated from the blood, or, after death, from the spleen and the gall-bladder.

The civil population has been equally free from it. The disease has, however, been raging in the German, Austrian, and Russian armies, and among the inhabitants of those countries as well.

In the prisoner's camps in Germany, as a result of a deplorable hygiene and the abandonment of the sick, large numbers of cases and deaths have occurred among soldiers of the Allied armies.

In Germany, at the present time, a hundred cases are reported monthly among the civil population. The German Army has not been spared, and many physicians also have succumbed to the disease.

During the first year of the war there were in Austria-Hungary, according to Jeanneret-Minkine, about 1500 cases of typhus monthly.

Serbia, during the present war, has of all countries been most cruelly scourged by typhus. Soldiers and inhabitants have succumbed in enormous numbers. It is estimated that typhus has claimed at least 135,000 victims, and 160 physicians have perished while attending to the sick. In one American ambulance eleven nurses out of fourteen were attacked.

The origin of this terrible epidemic was due to the 70,000 Austrian prisoners interned in Serbia, who brought the disease with them. It spread in every direction, and almost every house was stricken. It is estimated that one person out of every five was attacked. The mortality in the hospitals was 19 to 65 per cent. In Belgrade there were 7000 cases in less than six months. The towns of Valjevo, Nish, Monastir, and Uskub were most seriously affected.

It must not, therefore, be supposed that this infectious disease is extinct in these regions.

Apart from war-time, it has been and is still prevalent,

although by no means frequent, among the civil populations. In 1868 the natives of Algeria, being in a state of famine, had to be collected in relief stations, where the disease was not slow to make its appearance. It was then for the first time that cases of typhus were observed among Europeans who had been in contact with the starving Arabs, who were themselves, however, exempt from typhus, at all events in appearance.

A few sporadic cases are fairly often reported in Volhynia, Austria, and Holland.

Ireland and Norway are also subject to outbreaks. In Spain, Castellvi reported that he had, in 1909, observed 545 cases of typhus in Madrid. It Italy, in 1888, an epidemic caused 2099 deaths.

In France, in 1870-1871, 551 cases and 121 deaths were reported at Riantec, near Lorient. The epidemic continued for fourteen months.

At Rouisan in 1877 there were 165 cases; in the Îles Molènes in 1878, 282 cases and 12 deaths; in the Île Tudy, in 1891, 80 cases.

In 1892-1893 scattered cases of typhus appeared, first in Amiens, in a night shelter for vagrants and tramps, then in Abbeville, Pontoise, Beauvais, Evreux, Mayenne, Saint-Denis, Paris, Dieppe, Lille, Havre, and Bordeaux (among the workers of the port and in the Nanterre prison).

In all 684 cases were reported. About 100 physicians, nuns, and assistants were infected in the north of France.

Between 1903 and 1912 (inclusive) there were 209 cases of typhus in France.

In Russia a serious epidemic was reported in Petrograd during the winter of 1864-1865 (causing nearly 12,000 deaths). Between 1905 and 1911 there were 665,865 cases and 54,533 deaths from typhus (Pottevin).

In England, between 1899 and 1913, there were only 390 deaths. In Ireland, during the same period, there were 1043 deaths. In 1914 there were 37.

In Sweden, since the epidemic of 1875, which caused 1918 cases, typhus has become much less frequent.

In Germany, the very serious epidemics which occurred among the French armies in 1813 appeared among the inhabitants also: 18,000 cases and 3024 deaths were recorded in Bavaria, between November, 1813, and June, 1814. In the kingdom of Prussia alone the epidemic caused 200,000 deaths in 1813.

There were epidemics in Prussia in 1867-1869, and in Berlin; in Koenigsberg in 1880-1882 (672 cases and 97 deaths). Silesia remained the most virulent centre of the disease. In 1868-1869 there were 1333 cases in that province; in 1878-1879, 600 cases. Between 1877 and 1910, 14,655 persons infected with typhus were treated in the German hospitals (Pottevin). Cases were reported in Silesia (district of Oppeln) in 1912, 1913, and 1914.

Austria and, above all, Galicia and Poland have been particularly infested by typhus. Between 1904 and 1913 (inclusive) Galicia was responsible for 24,107 cases of typhus, and 2282 deaths.

The Bukovina, Bohemia, and Bosnia-Herzegovina are not exempt. The disease reappeared at the commencement of the war of 1914, among the Austrian troops and in most of the provinces. The Austrian prisoners, as has been stated, carried it into Serbia.

In Rumania typhus is very rare. However, during the first three months of the war there were forty cases in Bukarest. There is typhus in Bulgaria. It was prevalent among the troops during the war of 1912-1913, above all at Chataldja and Adrianople, and at Philipopolis, in Macedonia, in July, 1914.

In 1914, fifty-one cases and thirty-one deaths were recorded at Salonika. Fresh cases made their appearance in 1915.

Turkey, in which country there is a lack of exact statistical information, is the accustomed home of typhus epidemics. Cases have been observed in Constantinople, Smyrna, Trebizond, Adalia, Konieh, and

Karpout, and at Gallipoli, in 1914-1915 both in the army and among the civil population of the country.

In Persia, Ispahan, Hamadan, etc., were visited during the year 1914 by an epidemic of typhus.

In the north of Africa, notably in Algeria, Tunis and Morocco, typhus prevails in a mildly sporadic condition, with occasional epidemic outbreaks, in the native *douars*. Its propagation is facilitated by the customs of the country; the sick man, supported under the arms, walks about the streets to combat the fever, and in the midst of an epidemic typhus patients in the eruptive stage have been seen moving about the streets of Tlemcen (Dauthuile). The Arabs and vagrants, in return for a trifling payment, sleep packed together in the Moorish cafés and *fondouks*, where they infect one another.

Cases of typhus affecting Europeans have been reported from Western Morocco also, and rigorous prophylactic measures had to be taken to eradicate the disease.

Egypt yearly furnishes a large number of cases. In 1914 there were 9350 cases and 2634 deaths. During the first six months of 1915 there were 14,505 cases and 3398 deaths. The disease attacks the natives more particularly.

In Central America, in Mexico, typhus is known by the name of *tabardillo*. Between 1904 and 1913 there were 56,719 cases and 14,758 deaths.

In the United States typhus is endemic (Nathan Brill), introduced, or maintained by immigrants.

CHAPTER XIX

ETIOLOGY OF TYPHUS

Predisposing Causes

Typhus does not appear to spare any race or races. All (Latin, Slav, Anglo-Saxon, Indian, Chinese, etc.) pay it tribute. The Arabs and Turks, however, are its chosen victims.

The malady is more benign in children and adolescents. Its gravity increases considerably after the age of thirty or forty.

The mortality in children is 5 per cent.; in adults it is 8 to 20 per cent., and often more. It increases with age.

According to Murchison the mortality per 100 patients is:

Over 30 years	35 per cent.
,, 40 ,, ...	45 ,,
,, 50 ,, ...	53 ,,
,, 60 ,, ...	67 ,,

During the Russo-Turkish War the mortality among assistant surgeons, orderlies, and the men of the supply trains was at its maximum between twenty-five to forty years of age.

The two sexes are not attacked with equal frequency, women being more frequently attacked than men (Rochard).

Typhus is a malady of cold or temperate countries. It is most frequently observed during the cold season, as was seen during the Russo-Turkish War. According to Brill, the severe form is prevalent more especially in winter; the attenuated form in summer. In Mexico

typhus does not exist in cities where the temperature is high, such as Vera-Cruz.

At the time of the Serbian epidemic the disease was checked in summer.

Typhus has been intensely prevalent in Serbia during the present war, from the end of December, 1914, to July, 1915. The first cases made their appearance in September, chiefly among the patients in the typhoid wards, in the hospital for contagious diseases at Valjevo. It was during the retreat to Albania, however, that it attained its greatest severity. The epidemic was "the most serious that Europe has ever experienced" (Petrovich). In March there was no longer the least little hamlet untouched by the scourge. The mass of favouring causes which are most commonly incriminated were all united in the case of this unhappy people.

Crowding results in the readier propagation of the germ and its agents of transmission. This explains why typhus spread so rapidly through the prisoner's camps in Germany during the present war.

Famine and physiological want have always been incriminated as the adjuvants of typhus. Hence the name of "famine fever," "famine typhus," which the old physicians gave the malady. Still, it is important to note that these depressing conditions go hand in hand with the lack of personal hygiene and the hygiene of clothes, individual uncleanliness, and infection by means of vermin, which play such an important part.

Anæmia, fatigue, privation, and cachexia, moreover, give the clinical development of typhus a special and particularly serious character, which has been observed in all those epidemics which have been associated with famine. Under these circumstances the bastard non-febrile forms are equally numerous, and because their exact nature is habitually misunderstood they contribute to maintain the frequency of epidemic cases.

In Algeria, above all, in the region contiguous to

Morocco, typhus maintains itself in the numerous encampments in which the natives of Morocco live in promiscuity, without hygienic precautions. A serious epidemic broke out in the province of Oran, in 1906, on the occasion of the important construction works of the railway to Lalla-Marnia.

The harvest in the Algerian Tel had attracted also numbers of natives from Tafilalet or Marakeesh, where the disease was prevalent. A number of physicians died. Driven by famine, the cachectic natives of Morocco, arriving in great numbers, brought the malady into the workshops, into the houses of the railway workers and the agricultural labourers, and infected the beggars and the indigent (Surgeon-Major Duthuile).

Whichever races or countries are infected, typhus furnishes a body of predisposing causes the nature of which is fairly uniform. It persists more especially among poor and uncleanly populations. When it attacks the civilised inhabitants it does so, in a way, accidentally. It dies out on the spot instead of giving rise to a true epidemic state.

In famine-stricken countries, on the other hand, and also in armies, its appearance may be terribly serious, on account of its progressive extension.

This was exemplified in the case of the prisoners interned in the German camps in 1915. Their nourishment was extremely bad in quality, extremely insufficient, and only partially assimilable. As a result the prisoners fell into a positive state of inanition (Davy and Brown, Leonetti). They received a bath only once a month, or once in two or three months, and, covered with vermin, were packed into small, insanitary huts, which provided six cubic metres of air per head ; the atmosphere was fetid. All these factors predisposed them to infection in the highest degree.

In the camp at Langensalza, in April, 1915, nearly the whole of the 1000 prisoners contracted typhus (Leonetti). It is said that on an average thirty-five men died daily. They were ill-attended, without

medicines, and their clothing was insufficiently disinfected. In the camp at Niederzweren typhus also made serious ravages. It was only when the epidemic attacked the civil population and the garrison that precautions were finally taken. At Erfurt there were 600 cases among 20,000 prisoners. In the camp at Gustrow the hygienic conditions were equally deplorable. The 12,000 prisoners, suffering from cold and hunger, were crowded together on mouldy straw, with a single blanket apiece, which was worn, and often torn.

CHAPTER XX

ETIOLOGY OF TYPHUS—*continued*

Determining Causes

MANY bacteriological researches have been undertaken with a view to isolating the pathogenic agent of typhus; this, however, is still unknown.[1] Cultivation of the blood on the usual media gives negative results. Thoinot and Calmette have described a flagellated parasite; Bruhl and Dubief a diplococcus; Gottschlick a protozoon, like an endoglobular piroplasma, or free and motile; Plotz a special bacillus, etc.

Ricketts and Wilder have reported the presence in the blood of certain rare bodies, always free, which Gavino and Girard have recognised under the aspect of "bacilliform bodies," 2μ by $1{\cdot}2\mu$ in diameter, exhibiting at the extremities two small masses, rounded, like the weights of dumb-bells; the significance of these is, however, extremely obscure, and their etiological functions have not yet been demonstrated.

Proescher stained blood-smears for five to ten hours with carbonate of methylene blue (1 per cent.), and carbolic acid (1 per cent.); he then saw very fine diplococci and diplobacilli from $0{\cdot}2\mu$ to $0{\cdot}3\mu$ in length, enclosed in the endothelial cells of the blood-vessels.

There is reason to believe that the virus of typhus belongs to the group of *invisible* or *filterable* viruses. The ultramicroscope reveals nothing in the patient's blood.

[1] Quite recently a spirochæte has been described in Japan in cases of typhus, but this requires confirmation.—ED.

The inoculation of typhus blood gives rise to the malady. Motshovkovsky, after five fruitless experiments upon himself, obtained a positive result the sixth time. Blood was drawn from a young girl suffering from typhus, and on the tenth day presenting numerous petechiæ. Motshovkovsky was inoculated with this blood. The incubation period lasted eighteen days, after which time he was attacked by violent shivering, fever (104·9°), delirium, and a comatose state which lasted for fourteen days, accompanied by a petechial eruption, bronchitis, and myocarditis.

In Mexico, where typhus is frequently prevalent, and is known as *tabardillo*, Otero inoculated four healthy individuals with the blood of typhus patients. In one case the injection of 0·2 c.c. of blood from a *tabardillo* patient into a man whose physiological condition was poor determined a serious form of typhus after eleven days' incubation.

Yersin and Vassal, in Indo-China, succeeded in inoculating two coolies with typhus, by means of blood drawn on the second day of the malady. The incubation period lasted fourteen days in one case, twenty-one in the other.

From these experiments we may therefore conclude that the parasite of typhus exists in the blood of the patient.

Exact confirmation of this statement has been obtained by the admirable investigations of Ch. Nicolle, Comte and Conseil, of Tunis.

These experts have established the fact that the higher apes are receptive to the typhus virus, and form the most favourable subjects for inoculation. They inoculated a chimpanzee with the blood of a typhus patient on the third day ; after the lapse of twenty-four hours the ape was suffering from fever, and on the fifth day the eruption appeared on the face, ears, and flanks.

This was not a case of a lesion of a toxic order, for the blood of this ape was itself virulent and inoculable on the fourth day, when it was injected into a Chinese

macacque, which developed typhus after an incubation period of thirteen days. It was not inoculable before the fourth day.

To sum up, the injection of a cubic centimetre of the blood of a typhus patient suffices to cause the certain development of typhus in the chimpanzee. The symptoms and the development of the disease recall infantile typhus ; the fundamental characteristic is fever. Death may result.

In this way innumerable transfers may be realised. After recovery the apes are immune. The serum of a man or an ape possesses, after recovery, preventive and curative properties as regards the ape, but does not retain them for more than fifteen to twenty-five days.

The blood is virulent two days before the fever commences, and while the fever lasts, and for a few days longer (Nicolle, Comte, and Conseil). A temperature of 55° C. applied for fifteen minutes (Gavino and Girard), or even of 50° C. (Nicolle) kills the virus. The incubation period of typhus in apes is from four to twenty-eight days ; it averages from five to eight days. The typhus of apes resembles that of man (injection of the conjunctivæ, exanthemata, fever, commencing suddenly or progressive, anorexia, prostration, etc.).

In Mexico, Goldberger and Anderson, and then Ricketts and Wilder, shortly after Ch. Nicolle and his collaborators had completed the above experiments, confirmed the inoculability of the typhus virus in the *Macacus rhesus*, the incubation period being five to twelve days. The animals recovered. The initial inoculation was almost always positive in its results. Ricketts and Wilder employed the serum derived from defibrinated blood subjected to centrifugalisation (Nicolle allowed the blood to coagulate).

Gavino and Girard successfully repeated the whole of the investigations described above upon *Atelles vellerosus*.

Diluting the blood of patients and filtering it through a Berkefeld filter, Ricketts and Wilder were unable to

provoke the disease by inoculation; but the portion left upon the filter was virulent.

Nicolle succeeded in provoking the disease by the injection of filtered blood once out of six times. Campbell failed.

The usual "laboratory animals" have usually been regarded as refractory to typhus, but Nicolle has demonstrated that the guinea-pig is sensitive to the virus. The infection is revealed by one symptom only, and that an inconstant one—fever, which lasts eight to twelve days, commencing a week after inoculation. During this period the blood is virulent if injected into the monkey or the guinea-pig, even if the animal providing the blood is not suffering from fever. Transfers through alternate monkeys and guinea-pigs can be effected indefinitely.

On separating the various elements of the blood, Nicolle found that the white corpuscles are extremely virulent in infinitesimal doses; the plasma is less so; the red corpuscles are inactive.

The typhus virus appears, therefore, to be localised in the leucocytes of the blood.[1]

The foregoing discoveries already throw an interesting light on the etiology of typhus. We are forced to ask ourselves what, considering the contagiousness of typhus, is the medium of contagion in the patient. Is contagion effected by the normal or pathological secretions, by the saliva, the expectorations, the urine, etc.? It does not seem that this is the case, contrary to the opinion which was formerly current. Netter and Nicolle, in this connection, deny that the expectorations play any part.

On the other hand, the plainly demonstrated existence of the parasite in the blood would lead us to suppose that the transmission of the virus, as in

[1] The blood of typhus patients and of the animals inoculated reveals necrosis of the polynuclear neutrophiles, sometimes to a considerable extent. The nucleus has a mulberry-like appearance, and the protoplasm shows granulations of a lilac colour (Nicolle).

malaria and yellow fever, is effected by an ectoparasite or by the bites of insects.

Nicolle has found that the bite of the mosquito, the tick, the stomoxys, the louse, the flea or the bug, after the insect has sucked the blood of typhus patients, is without effect upon the normal monkey.

In the phosphate mines of Tunisia, where the fleas are very abundant and bite everybody, only the natives suffer from typhus.

Mosquitoes and ticks do not exist in winter, nor in spring, seasons at which typhus is especially prevalent. Lastly in the prisoner's camps in Germany where typhus was prevalent, there were swarms of lice, but no fleas or bugs.

Ricketts and Wilder have also found that neither fleas nor bugs can transmit typhus to the monkey. Nicolle, Conseil and Comte have proved that it is the *louse*, and particularly *Pediculus vestimenti* which serves as the agent of inoculation. In more than 800 cases of typhus observed in Tunis in 1908, $\frac{15}{16}$ of the patients suffered from parasites, or were vagrants exposed to the bites of lice. Their contagiousness disappeared when they had been bathed and given a change of linen. In four cases of typhus the malady had assuredly followed the bites of lice.

Experimentation has, for that matter, verified the truth of this proposition. Lice nourished on the blood of a monkey (Chinese bonnet monkey), and left without food for eight hours, when transferred to another monkey (a macacque) infected it with typhus.

Ricketts and Wilder (the first of these scientists dying of typhus on the occasion of these experiments) also obtained positive infections with body-lice which had been placed on typhus patients, or infected apes, or monkeys, and were then transferred to healthy animals. The same effect was produced by taking the excrement of lice and inoculating it under the skin, or by crushing the lice themselves and inoculating them,

the lice having sucked the blood of a typhus patient three days earlier. Having collected a thousand young lice, the offspring of 140 adult lice, fed on the blood of a typhus patient, Ricketts and Wilder reared them to the adult state. This generation produced lice which, placed upon a macaque, caused no infection. But afterwards this monkey was refractory to a very powerful inoculation.

According to Nicolle the bite of the louse is pathogenic only from the fourth to the seventh day after an infective meal.

Pediculus vestimenti is thus *the intermediate host, as well as the agent of transmission of typhus. When the louse has absorbed the blood of a typhus patient the parasite of typhus infects the louse itself after the lapse of a few days. Possibly this infection causes an actual disease in the louse. At all events, a multiplication of the typhus germ takes place, and after a period of a few days the germ has become inoculable into man. Perhaps it is in the louse itself that we might most fruitfully search for the virus.*

It may be concluded, then, that the agent of transmission for the virus is the body-louse, after the insect has fed upon a person affected by the disease. The blood of the patient is virulent during the whole course of the malady, and even for some days before the onset, and a few days after recovery.

The infectious germ survives, maintaining its virulence, in the alimentary canal of the louse, multiplies there, and undergoes a special development; it is inoculated by the louse, or by its very profuse excrement deposited on a cutaneous excoriation. Experiments upon monkeys have verified this latter mode of contagion.

The louse is capable of transmitting typhus for a few days only. But it may once more become contagious after a fresh infective meal. Finally, its offspring may sometimes transmit the infection (Nicolle).

Examples cited by Jeanneret-Minkine show that the bite of the louse may be much more certainly infective than involuntary inoculation with instruments polluted by the blood of the typhus patient. This was exemplified by an attendant in a post-mortem room, who remained unaffected in spite of excoriations and daily wounds which he did not disinfect. However, this man contracted typhus later, while attending on a patient.

Cases have been cited in which typhus seems to have developed independently of the bites of *Pediculus vestimenti*. Physicians attending typhus patients, but protected by rubber gloves and hermetic overalls and boots, have nevertheless contracted typhus. This fact, if verified, would seem to prove that the louse is not the only agent of transmission (Larrieu). Still, it appears to be demonstrated that one single bite of an infected louse is capable of provoking typhus. It is easy to understand that this bite might pass unnoticed, especially as the louse bites almost immediately, if hungry.

Of the three species, *P. capitis*, *P. pubis*, and *P. vestimenti*, the latter is by far the most usual agent of transmission. *P. capitis*, having bitten a typhus patient, retains the virus for at least twenty hours, and if placed upon a monkey gives it typhus (Anderson and Goldberger). *P. vestimenti*, in the adult state, attains a length of 3 and even 4 millimetres (Jeanneret-Minkine). It has three pairs of limbs, by means of which it fixes itself upon clothing or moves about. It lodges in the folds and seams of clothing, or upon the surface itself. It lays its eggs on the fibres of cotton or woollen garments, but it can also deposit them on the hairs of the body. From its birth, which takes place in six or seven days, the insect bites the human host. The eggs may also be laid on the covers of mattresses. The best temperature for hatching is 82·4° F. It is retarded by temperatures of 76° or 95° to 104°.

P. vestimenti lives only upon blood, and dies if deprived of it for two to five days. It does not settle on the skin except while puncturing it for the purpose of obtaining nourishment. Extremely avid of blood, it absorbs excessive quantities of it, even as much as a milligramme. This explains the abundance of its dejecta, by means of which infection may occur if the victim scratches himself.

The capacity of multiplication possessed by *P. vestimenti* is, according to Jeanneret-Minkine, considerable, for in one month a couple may give birth to more than 2000 descendants. Moreover, among the Arabs one sometimes sees persons whose bodies and garments are entirely covered with these parasites.

When it is hungry the louse is capable of deserting abandoned garments or straw bedding and of going in search of its food. It can therefore make its way, although slowly, toward an adjacent human being. This is certainly what takes place in cantonments and trenches, where men who are not infested may be contaminated by sleeping on straw.

The body-louse does not survive in hot climates. This has been observed in Mexico. At Tampico the louse-infested labourers who come in search of work are rid of their lice in five days, although no measures have been taken to destroy them. The serious epidemic which was lately raging in Serbia was arrested in spring "because at this season the lice had disappeared" (Hirschfeld).

Numerous examples, recorded by the medical history of typhus, testify to the excessive contagiousness of the disease.

The introduction of the germ by a single patient may give rise to a serious epidemic. This was seen on the occasion of the epidemic of 1893. Thoinot and Ribierre have summarised the part played by contagion in respect of the cases which occurred in Paris at this time in an instructive table.

Twenty vagrants suffering from typhus (in Paris) infected :

At the poorhouse	In asylums, police-stations, and lodging-houses	At the Palais de Justice
41 persons under detention, 4 warders	42 vagrants, 3 lodging-house keepers, 3 other persons	1 recorder

These typhus patients, nursed in the hospitals, caused 23 cases.

A total of 137 persons infected.

Typhus, as we have seen, is transmissible during the prodromal period. In 1893, at Lille, fifteen persons who had come into contact with a prisoner contracted typhus. Now the prisoner himself did not develop typhus until several days later. Typhus is also transmissible after recovery. At the same period a female patient, Mme F——, of Amiens, carefully isolated, having recovered from a benign form of typhus, left hospital and communicated the disease to another woman who called to see her. A few days later she went to Dreux, and introduced the disease there.

The facts already expounded as to the function of the *Pediculus* give us the explanation of the delayed transmission of the disease by lice which have drawn blood at the end of the febrile period, or even several days later, when the blood was still infective. The louse itself retains the germ of typhus for several days, and this after a definite period of incubation.

It will therefore be understood how typhus may be propagated not only by those who have been in direct contact with the patient, but also by those who have come into contact with his clothes, his body-linen, his bedding, his mattresses, his straw bedding, etc.

It should, however, be remembered that *P. vestimenti* dies after the lapse of a few days if unable to nourish itself upon blood.

The propagation of typhus has been reported in the case of orderlies who have handled the clothing of typhus patients, those who have charge of the cloak-room in hospitals, and those who repair soldiers' overcoats if

these have not been disinfected. Contagion may also be effected in railway carriages, public vehicles, prisons, etc., through the medium of lice in search of a human host. However, the cause of infection may remain uncertain. This was the case with an advocate who contracted typhus in 1895, at Lille, in the Palais de Justice, where vagrants and thieves were tried. He died, as did his secretary. It was impossible to discover the source of contagion.[1]

The older generation of physicians laid great stress on the transmission of typhus by famishing masses of persons who themselves were apparently unaffected (Périer, Vital, Maurin). Kelsch has confirmed this hypothesis. The episode of the *Shea-Gehald*, cited by Griesinger, is well known. This vessel sailed from Egypt in November, 1860, arriving at Liverpool on the 16th February following. She carried a native crew, ill-fed, suffering from diarrhœa and sea-sickness, but with no case of typhus among them. Now three persons who visited the vessel on her arrival contracted typhus ; one of them died. Some sailors sent to the hospitals on account of various affections carried typhus thither : 1 physician, 1 student, 2 male nurses, 2 porters and 17 patients were attacked. The sailors, to the number of 340, visited the baths ; 3 bath-house attendants out of 6 contracted typhus, etc.

It seems highly probable that there was typhus among these men, but that it existed in some ill-defined form such as is frequently observed among famine-stricken or ill-nourished persons. Moreover, eleven deaths had occurred during the voyage through the Mediterranean.

These unusual forms of typhus, without fever, but with diarrhœa, loss of strength, and early or sudden death, have been observed during all epidemics, and in particular during the Serbian epidemic of 1915.

[1] Why not the louse ? Vagrants and thieves are notoriously lousy, and it seems highly probable that the advocate and the secretary were bitten by infected lice introduced by these people.—Ed.

Numbers of these cases were variously diagnosed as physiological want, dysentery, etc.

The epidemiological importance of these bastard forms need not be emphasised. A precise inquiry should always be made in order to trace the antecedents of such cases. As we have seen, this is not always easy to establish. It often happens that the first cases are unrecognised. At other times patients or convalescents are sent into neighbouring hospitals, and are discharged too early, and without disinfection. These patients spread typhus wherever they go by means of the lice which they carry with them.

CHAPTER XXI

PROPHYLAXIS OF TYPHUS

Although typhus has not hitherto been observed in the French and British armies, and although the civil population has been free from it, we may consider that *this infectious disease*, which is prevalent in the armies of the east and south-east of Europe, *is always a menace to our armies*, because of the conditions of life to which the men in the trenches and cantonments at the front are subjected, the multiplicity of human contacts, and the profusion of ectoparasites which afflict our soldiers. It is therefore important thoroughly to understand the prophylactic measures to be opposed to this disease.

The campaign against lice remains the most profitable means of prophylaxis, and that which should be most urgently insisted upon. This point will be specially dealt with later.

Wherever the disease has manifested itself an early notification should be made of every case. The patient should be strictly isolated in a special ward, in a portable building in winter, or in a tent in summer.

Immediately upon admittance the hair of the head should be cropped, the hair of the body shaved, and both should be burned. The patient should be placed in a bath containing corrosive sublimate, washed, soaped, and scrubbed, and all his parasites destroyed. His clothes should be burned or sent to the oven directly upon his admittance to hospital. If this is not done they should be plunged immediately into boiling water containing washing-soda.

All persons who have been in contact with the patient, and, above all, those who are infested with lice, should be placed under supervision for a period of fifteen days.

This precaution, therefore, applies to families, ships' crews, or passengers, military units, workshops, Arab *douars*, prisons, etc. All suspects should undergo a scrupulous insect disinfection, by means of antiseptic baths, soaping, etc. The hair and beard should be cropped or shaved, while clothing, underclothing, boots or shoes, caps, etc., are to be sterilised or destroyed by fire.

The quarters inhabited by the patient, his linen, sheets, mattresses, bedding, etc., must be subjected to disinfection; the linen and articles to be sent to the stove should be placed in special sacks; the infected premises should be disinfected with sulphur gas; articles of no value, such as rubbish, worn clothing, mats, carpets, etc., should be destroyed by fire; the floor should be washed with a boiling solution of soda (1 per cent.). The persons entrusted with the work of disinfection must wear special clothing and rubber gloves.

On board ship the same precautions should be taken, while passengers and crew are to be subjected to sanitary supervision for fifteen days. Carriers of vermin must be placed under observation for the same period.

In hospitals the nurses or orderlies should be selected from the younger members of the staff; those who have already had typhus should be chosen, if such are available. They should wear special clothing: blouses closing tightly at the neck and wrists, rubber gloves, trousers fitting closely at the ankles, with well-laced boots, and a head-covering or "helmet" of linen. In the British hospitals in Serbia the staff wore a single garment, a sort of "combination," closed at the neck, buttoning at the shoulders, with the ends of the trousers shaped to enclose the feet; the latter were shod with sandals. Nurses or orderlies must not relax their precautions, experience having frequently shown that after some time they are apt to become forgetful, and so contract the disease.

Blouses, aprons, head-coverings, etc., should be removed by the attendants when they leave the ward or go to meals. A change of clothing is advisable each time a fresh patient is admitted.

Instructions as to the means by which typhus is transmitted, and the part played by lice in the spread of contagion, should be issued, and everyone should be reminded of the difficulty of protecting themselves against the bite of the louse, and of all the precautions to be taken to avoid them, particularly on the arrival of patients who have not as yet been disinfected. Nurses, doctors, and attendants should take an antiseptic bath daily (containing cresol or corrosive sublimate).

No specific prophylaxis has so far been discovered.

Anderson, however, has suggested that persons exposed to typhus would act prudently by getting themselves inoculated with attenuated typhus (Brill's disease).

Nicolle attempted to immunise twenty Serbian soldiers and eighteen other persons by injecting half a cubic centimetre of serum from an infected guinea-pig, followed, at an interval of nine days, by one cubic centimetre. He obtained satisfactory results, which should encourage others to repeat such experiments.

The Campaign against Lice

The transmission of typhus by the pediculi necessitates, as its prophylactic consequence, the "disinsectification" or "disinsectisation" of the patient, his entourage, and all those who approach him or have approached him.

Pediculus vestimenti lives more particularly in or on the surface of clothing. The frequency of vermin among soldiers in the field, even among those who take precautions as to cleanliness,[1] would constitute a

[1] According to Peacock, 4·9 per cent. of the British soldiers have no lice; 41·9 per cent. have very few. The rest suffer from them in varying degrees.

formidable factor of propagation were the virus to be imported. It is important, therefore, to describe the various means designed to destroy these parasites.

1. For the individual himself numerous means have been recommended: swabbing with petrol, xylol, benzine, essence of aniseed, turpentine, ether, chloroform, essence of cloves, or of eucalyptus, etc. These volatile liquids, it is to be remembered, are inflammable; nevertheless, they are really efficacious, especially xylol; the nits often resist benzine.

Frictions with anisol (methyl-phenyl-ether) may be recommended. A mixture of oil and petrol, less volatile, is equally useful. The mixture:

Naphthol + benzol + NH_3 . . .	} equal parts
Benzine	

pulverised on the skin (and clothing) with an ordinary pulveriser effectually destroys lice. This means is recommended in the Italian Army by Guido Izar.

Sachets for personal wear, containing naphthaline and camphor, placed under the armpits or at the waist, are of little use. Sulphur has no effect, and the same is true of powdered pyrethrum.

The British Army makes considerable use of the N.C.I. powder, composed as follows:—

Naphthaline	96 grammes
Creosote	2 ,,
Iodoform	2 ,,

This powder is applied to the skin, shirts, trousers, etc., and renewed every five days. It does not kill eggs with certainty.

Swellengrebel has recommended anisol, globol (para-dichloro-benzene), which is non-toxic, or lausofane, a cyclo-hexanon base and cyclo-hexanon associated, in powder or alcoholic solution, with which the skin is soaked or covered while the clothing is being disinfected.

The hair of the head and body should be cropped or shaved, and the body should be soaped with soft soap

or cresol soap; this treatment should be continued for a fortnight. Brumpt recommends washing with three parts of soft soap mixed with one part of glycerine.

The nits of *P. pubis* are destroyed by a solution of corrosive sublimate (1 in 1000), to which 30 per cent. of acetic acid has been added (Brumpt).

Excellent results are also obtained by swabbing the pubic and axillary regions with strong alcohol, in which 10 per cent. of β. naphthol has been dissolved.

All these local operations should be followed by a bath.

After each bath, disinfected clothing should be donned. The process of insect disinfection must be carefully carried out, for an imperfectly cleansed person may in a few days reinfect all his neighbours.

The hair of the head should be cropped very close, and soaked in a mixture of oil and petrol.

2. *The destruction of lice on clothing* is effected by means of heat, dry or moist, or by anti-parasitical vapours.

Lice are killed in three hours by a temperature of 45° C. (113° F.); in one and a half hours by a temperature of 50° C. (122° F.); in twenty or thirty minutes by a temperature of 60° C. (140° F.); and in ten minutes by a temperature of 80° C. (176° F.).

The nits are more resistant.

Dry heat applied by a hot iron effectually kills lice and eggs on clothing, but the iron must be carefully passed several times along all the seams.

Boiling destroys the parasites. Ordinary coppers or lye-washing machines of 80 litres capacity are employed, and give excellent results (Voyotte).

Live lice, placed in test-tubes in the midst of clothing, are killed by this process in three or four minutes; in ten minutes the embryos in the nits are killed (Brumpt).

A note issued by the General Staff, *Direction de l'arrière*,[1] dated the 28th August 1916, suggests, as an emergency method of disinfecting clothing, the

[1] As distinguished from the medical service in the field.

employment of a barrel (as recommended by Surgeon-General Richard) placed above a saucepan or copper which is giving off steam. The bottom of the barrel is perforated to allow the steam to pass through.

The same note recommends the employment of Budan's device, which consists of two coppers or vats, of unequal size, one being placed over the other. The whole is heated by means of wood or coal.

Finally, a supply of steam may be employed (from a boiler or agricultural engine), the exhaust-pipe ending in a barrel containing the articles to be disinfected.

The Bordas process consists in passing steam through a worm contained in an ordinary barrel.

It is as well to use alkaline water in the coppers in order to increase its bactericidal power.

In Amsterdam the destruction of lice is effected by the vaporisation of ammonia (25 per cent.) in hermetically closed rooms.

In the German Army sulphuret of carbon is regarded as being possessed of great activity.

The employment of silken underclothing has been recommended in place of woollen or cotton articles, as the lice cannot effect a lodgment on silk.

When the articles have been sufficiently baked or steamed, they should be carefully dried before being worn again.

During the operation of disinfecting and drying the clothing and underclothing the carrier of the vermin himself may be shaved, disinfected, soaped, and bathed.

Thanks to these measures, typhus, which has made such serious ravages in Serbia, has been stamped out.

Rumania succeeded in protecting herself against the importation of typhus from Serbia, by means of adopting the same measures on the frontier, and by imposing a rigorous quarantine on immigrants.

It was the same with Greece. Travellers coming from contaminated countries received an inspection card, containing five divisions, on which the temperature was entered for five days. The traveller was

required to visit the physician under penalty of a heavy fine. Useful as it is, this measure is not infallible, for the incubation period of typhus may be much longer, and in infected subjects who are in a low physiological condition typhus may be apyretic.

The treatment of clothing by the vapour obtained by burning sulphur or sulphuret of carbon (CS_2, 90 per cent. ; stove alcohol, 5 per cent. ; water, 5 per cent.) destroys the parasites very effectively. The clothes are hung up in a carefully closed room or closet.

The vapour of formol is less reliable.

3. *The disinfection of rooms*, etc., can also be effected by the use of sulphurous acid (50 grammes per cubic metre), the vapour being applied for two or three hours.

The flooring may conceal lice derived from typhus patients, underclothing, healthy subjects, etc. In this case it is best to go over the planks and skirtings with petrol, or to wash them with alkaline boiling water.

The staff entrusted with the insect disinfection of lousy persons and their clothing must take all necessary precautions to avoid infection. They should wear special garments, frequently changed, and rubber gloves to handle the infested clothing. The latter may be collected by means of long tongs of wood or metal for transference to the stove or oven.

These precautions are particularly recommended during epidemics.

SECTION III

SYPHILIS AND THE ARMY

SYPHILIS AND THE ARMY

CHAPTER I

THE FREQUENCY OF SYPHILIS IN THE ARMY

ALL great movements of population—wars, pilgrimages, exhibitions—induce a recrudescence of contagious diseases in general. Venereal diseases in particular always become more frequent in time of war.

During the wars of the Revolution * venereal morbidity was estimated at a fourth of that of the entire army.

The present war, owing to the immensity of the armies engaged, its long duration, and the large numbers of men mobilised in munition works, seems likely to leave all previous wars far behind, as regards the frequency of venereal diseases.

Up to the present the statistics of the belligerent forces are unknown †; and, in any case, they could

* See Spick, "Scabies and Venereal Diseases in the Armies of the Revolution and of the Empire" (*Annales de dermatologie*, October, 1908, p. 593).

† Balzer ("Prophylaxis and Treatment of Venereal Diseases in Time of War," *Presse médicale*, October 14, 1915, p. 40) reports that, according to German statistics going to the end of February 1915, the German troops at this period, in Belgian territory alone, had already had 30,000 cases of venereal disease, whereas in the war of 1870–71 the total number of venereal cases had been 32,528, viz. 70·6 per 1,000 of the sick in hospital.

give but a feeble conception of this frequency, for they are most incomplete, for several reasons :

In the first place, medical inspection of men with the colours is not carried out with sufficient rigour to obtain accurate figures, for divers reasons.

And, on the other hand, it is not only amongst the fighting units that venereal diseases are to be found ; they occur also amongst convalescent soldiers, as well as amongst munition workers, who, from the health point of view, must be regarded as soldiers.

Consequently, syphilis is frequently seen in the base hospitals, without precise statistics being procurable : many of these centres do not report the venereal cases treated, others ignore them. Patients suffering from gonorrhœa or syphilis gladly take advantage of their leave to obtain treatment unknown to the doctor in charge, and often go to quacks.

As regards munition works, despite the most laudable efforts, medical supervision is most inadequate. As the result of various unfortunate influences, in the majority of cases, even a brief medical visit is not made, and, there is no doubt, a large number of venereal patients conceal their malady, and are either badly treated or not at all, to their own disadvantage and to the still greater detriment of society in general.

As far as I have been able to judge, from personal experience and from conversations with numerous military surgeons, as well as those attached to the dermato-venereological military staff, the frequency of gonorrhœa has been markedly increased since the war, especially in certain regions. Mauriac has shown that simple chancre has a tendency to increase at a time of any great shifting of population, but its occurrence does not appear to be above the average.

As regards syphilis, with which I am alone concerned here, in the opinion of every one, it has increased notably since the beginning of the war, and there appears to be almost constant augmentation.

As I have already stated, statistics give but a very incomplete idea of this, because they only comprise the cases observed in the military hospitals, and many escape notice ; further, in order to appreciate this augmented frequency, it would be necessary to obtain statistics made before the war in the same communities. But pre-war communities have been modified, or rather, one might say, turned upside down by mobilisation ; army corps in time of peace in no way resemble our regiments at the front, as regards composition, and there was nothing comparable to munition works in the industrial works of 1913.

The opinions of syphilologists are much more valuable than statistics. The unanimous opinion is that the *frequency of syphilis is much greater at the present time* than during the periods preceding the war : all my colleagues in Paris and the provinces, when consulted on this subject, agreed as to this.

I shall now merely give some statistics :

Gaucher,* out of 2,457 soldiers treated at his clinic from August 1914 to December 1915, for cutaneous or venereal affections, recorded 277 cases of recent syphilis, and, amongst 88 soldiers in the out-patient department, 24 cases of recent syphilis.

In the same clinic, from January 1st to July 31st, 1914, out of a total of 2,295 patients, he observed 276 chancres or recent syphilis—in round figures 300 cases of recent syphilis amongst 3,000 patients; and from August 14th, 1914, to December 31st, 1915, in the same clinic, 4,912 patients, both civil and military, amongst them being 793 cases of recent syphilis—say 800 out of 5,000 patients.

* Gaucher, " Venereal Diseases during the War in the Villemin Hospital and in its Annexes " (*Bulletin de l'Académie de Médecine*, March 28th, 1916, p. 352).

Gaucher and Bizard, " Statistics of Syphilis contracted by Soldiers since Mobilisation and treated in the Clinic of the Hospital St. Louis, August 1914—December 1915 " (*Annales des maladies vénériennes*, March 1916, p. 129).

If these two statistics given are translated into centesimal proportions, out of the total of cutaneous and venereal patients, they represent 12% of venereal patients before the war and 16% since the war, therefore an increase of 4% or of $\frac{1}{3}$, which is certainly less than the reality and does not convey an exact idea.

In a clinic of cutaneous and venereal diseases in a colonial army corps, out of a possible effective force of 60,000 men, Rousseau * treated 27 cases of syphilitic chancre, from March 12th to July 1st, 1916, which corresponds to 89 cases of contamination in a year, and there is reason to believe that he did not see all the cases.

The statistical material of venereal diseases in the French Army has only been collected since the year 1916, and for variable periods for the three venereal diseases. The adjoining table, compiled from information given me by the kind permission of Mr. Justin Godart, Under-Secretary of State Health Service to the Minister of War, gives the number of contaminations reported month by month by the medical men of the various sanitary departments.

As regards syphilis, this table shows the oscillations which occur in the frequency of the disease, and of the results of the prophylactic measures prescribed ; but it does not by any means comprise all the syphilitic contaminations which occur in a military population, for several reasons. Despite the orders given, a considerable number of hospitals do not furnish detailed reports ; while, on the other hand, large numbers of syphilitic chancres are unrecognised, as the result of the insufficiency of the medical visits paid to the regiments and depots ; others are treated unknown to the regimental doctors. Further, these statistics only include patients who were admitted to hospital for a syphilitic chancre and, in order to prevent errors and

* Rousseau, " Treatment and Prophylaxis of Syphilis in an Army Corps " (*Presse médicale*, October 23rd, 1916).

double entry, no record has been made of those patients who, on admission, showed secondary affections, their chancre having been unperceived, or unrecognised for one cause or another. Therefore, under the heading of simple chancre, a large number of mixed chancres are hidden, the syphilitic phase of which has escaped the statistics.

Finally, these statistics only include the troops

VENEREAL CONTAMINATIONS RELIEVED IN THE ARMY TROOPS AND ON THE LAND.

	Gonorrhœa.			Simple Chancre.			Syphilis.			Total of venereal contaminations.		
	In the Army.	In the Interior.	Total.	In the Army.	In the Interior.	Total.	In the Army.	In the Interior.	Total.	In the Army.	In the Interior.	Total.
January, 1916 .	—	—	—	—	—	—	250	1,210	1,460			
February ,, .	1,018	3,416	4,434	—	—	—	321	1,206	1,527			
March ,, .	641	3,257	3,898	—	—	—	170	843	1,013			
April ,, .	553	2,434	2,987	71	331	402	192	660	852	816	3,421	4,241
May ,, .	337	3,210	3,547	54	457	511	161	753	914	552	4,420	4,972
June ,, .	569	3,000	3,569	82	428	510	169	787	956	820	4,215	5,035
July ,, .	475	3,068	3,543	64	459	523	189	794	983	728	4,321	5,049
August ,, .	414	3,578	3,992	18	417	435	131	998	1,129	563	5,124	5,687

Note.—For the months of January and February, the number of cases of syphilis *in the Army* includes not only patients in hospital with syphilitic chancre, but also those suffering from secondary affections; in the interior since the Army started, note has only been made of those patients in hospital with syphilitic chancre.

present with the colours; no account is taken of the men mobilised in munition works. Up to the present there is, unfortunately, no record of the cases of syphilis among them; and these, from personal observations and the confirmation of numerous doctors, appear to be of enormous frequency.

For all these reasons, interesting as are the statistics of venereal diseases among the troops, in that they enable us to follow the variations of venereal con-

tamination, and appreciate the results of prophylactic measures, they give but a very incomplete idea of the frequency of syphilis amongst a military population. If it were possible to register the total number of contaminations, this would, I believe, work out at 4,000 to 5,000 per month, say 50,000 to 60,000 per annum, which for three years of war would make 150,000 to 180,000 contaminations.

Pautrier, chief of the venereological centre of the eighth district (Bourges), in February 1916, observed 724 cases of primary or secondary syphilis amongst hospital patients, or those who came to consult him. This centre had only been worked from the month of September 1915, that is, for the period of six months.

"If one considers," he says,* "that the venereological centre, unfortunately, does not yet receive all the cases of syphilis in the district, a certain number of patients being wrongly detained in general or regimental hospitals, while others suffer from syphilis unrecognised by the medical man or concealed by the patient, and if one must admit without exaggeration that this calculation, to be correct, should be multiplied by 4 or 5, one sees what an impressive total would be reached in the eighth district alone. By multiplying this number by that of twenty other territorial districts and adding the very considerable figure of the army zone, it is possible to conceive that the cases of syphilis contemporaneous with the war will not be reckoned by tens of thousands, but by hundreds of thousands."

He considers that 200,000 syphilitics will be a highly probable number.

* Pautrier, "On the General Organisation of Military Venereal Hospitals and of the Annexed Services." Report presented at the Meeting of the Heads of the Venereological Centres, held July 13th, 1916 (*Annales de dermatologie*, September 1916, p. 233).

CHAPTER II

ON THE ORIGIN OF SYPHILITIC CONTAGION IN THE ARMY

As may be supposed, the origins of syphilitic contagion in the Army are multiple.

It is frequently difficult to determine them. All patients do not lend themselves to investigation with equal readiness : some have contracted syphilis under circumstances which they do not care to divulge ; others refuse, from a spirit of chivalry, to denounce the woman who accorded them a favour, whether gratuitous or paid for ; some, on account of drunkenness, are unable to give either place, time of meeting, profession, or colour of the hair of their temporary partner ; while others, again, have had so many and such frequent adventures with different women that they are unable to blame one more than another.

Despite the difficulties of the inquiry, a certain number of soldiers have replied to the questions with apparent veracity, and medical men have been able to obtain information of sufficient accuracy.

Some of these inquiries have been published, and they contain a sufficient number of names to be of value, especially those of Jolivet and Carle.

Take first Jolivet's * inquiry, which contains a list of the first 100 venereal patients treated in an infectious hospital in the army zone, and the information he

* Jolivet, " Origin of the Contamination of 100 Venereal Patients treated in the Army Zone " (*Annales de dermatologie*, May 1916, p. 126).

was able to obtain as to the manner of their contamination.

	Syphilis.	Gonorrhœa.	Simple Chancre.
I.—Official Prostitution, 52%			
Houses	16	10	—
Meeting-houses	—	1	—
Licensed prostitutes	9	14	2
II.—Clandestine Prostitution, 48% :			
Married Women — Dressmakers	—	1	—
Married Women — Laundresses	1	1	—
Married Women — Publicans	1	—	—
Married Women — Profession unknown	2	2	—
Married Women — Legitimate wives	3	13	—
Married Women — Refugees	2	—	—
Legitimate mistresses	1	1	—
Laundresses	3	2	—
Work-women	2	4	—
Waitresses in cafés	1	4	—
III.—Category Undetermined	1	—	—
IV.—Extra-genital Contagion (?)	1	—	—
V.—Contagion from pederastic acts	—	—	2 (1 in army. 1 in hospital.)

Carle * has obtained statistics giving the mode of contamination of 291 men observed in the venereological centre of an army.

These two statistics are particularly interesting, because they both of them treat of contaminations incurred as much in the army zone as in the interior ; thus allowing comparison of the mode of syphilitic dissemination in two entirely different centres.

The following statistics, prepared by Madame Govaerts with scrupulous accuracy, record 165 syphilitic men observed in my clinic in the St. Louis Hospital, from February 15th to August 15th, 1916, and in these cases it was possible to trace the origin of contamination.

* Carle, " Three Months' Work in the Dermatological and Venereological Sections of an Army Ambulance. Statistical and critical study " (*Archives de Médecine et de Pharmacie militaires*, June 1916, p. 865).

Carle, " Prophylaxis of Venereal Diseases in the Army. Measures taken, Measures to be undertaken." Report at the Meeting of the Heads of the Venereological Centres, July 13th, 1916. (*Annales des maladies vénériennes*, September 1916, p. 536.)

The statistics refer to both military and civil patients; I thought it better to combine them in the same table, in order to show that, in the interior, the majority of syphilitic contaminations are due to prostitution, amongst the civil as well as amongst the military population.

It is interesting to determine the source of syphi-

—	General Total.	Army Zone.			Interior.		
		Total.	Gonorrhœa.	Syphilis.	Total.	Gonorrhœa.	Syphilis.
Legitimate wives (to their husbands) .	12	1	1	—	11	7	4
Married women (townswomen and farmers' wives) . .	43	31	24	7	12	7	5
Work-women .	24	14	8	6	10	5	5
Servants and cooks . .	13	5	3	2	8	5	3
Farm-girls, or girls met on farms . .	17	15	8	7	2	2	—
Waitresses .	33	12	7	5	21	6	15
Landladies .	78	17	10	7	61	40	21
Professionals, either licensed or clandestine	71	18	14	4	53	40	13
Total . .	291	113	75	38	178	112	66

litic contagion separately in the different military classes : soldiers at the front, those in the depots and sedentary services, and men mobilised in munition works.

Men at the front may be contaminated either in the Army or the interior ; statistics show that they become affected much more frequently in the interior than in the army zone.

SOURCE OF CONTAMINATION IN 165 SYPHILITIC PATIENTS OBSERVED IN MY CLINIC
(February 15th to August 15th, 1916)

Class of Patients.	General Total.	Professionals.	Women met in restaurants or hotels.	Probable contamination by professionals: Patient could not or would not give information.	Probable contamination by professionals: Patient denied extra-conjugal intercourse.	Workwomen.	Married Women.	Wives or mistresses with whom patient had lived for a long time.
Military . . .	31	20	1	2	1	3	3	1 (wife)
Mobilised workmen .	21	12	1	2	3	2	—	1 (mistress)
Rejoined . .	37	22	1	3	1	4	3	3 (mistresses)
Young men not yet called up; Extensions; Civilians, 76.								
16 to 20 years of age .	24	15	2	—	—	6	1	
3 of 20 ,, ,,								
7 ,, 19 ,, ,,								
8 ,, 18 ,, ,,								
4 ,, 17 ,, ,,								
2 ,, 16 ,, ,,								
20 to 50 years of age .	42	28	1	5	1	4	1	1 (wife)
Half of these are of foreign nationality	—	—	—	—	—	—	—	1 (mistress)
50 to 73 years of age .	10	2	—	3	2	2	1	
7 of 50 to 60 yrs. of age								
1 ,, 64 ,, ,, ,,								
1 ,, 66 ,, ,, ,,								
1 ,, 73 ,, ,, ,,								
Total . .	—	99	6	15	8	21	9	7

Jolivet, whose inquiry yielded 100 cases of venereal disease, observed in an infectious hospital near the front, gives the following table :

		Syphilis.	Gonorrhœa.	Simple Chancre.
Men contaminated in the army zone (24%) .		11	11	2
Men contaminated in the interior (76%) .	In the depots .	24	13	1
	On leave	8	29	1

Carle, out of 291 men under observation in the venereological centre of the Army (see Table on page 9), takes 178, *i.e.* 61%, as having been contaminated in

the interior. In a series of 238 cases, more recently observed, he counts 170 contaminations coming from the interior, *i.e.* 71%.

In adding together the totals of these three statistics, out of 629 cases of venereal disease, 524 contagions are from the interior, *i.e.* 73·6%.

Tzanck has communicated the following statistics to me ; they were obtained in a military venereal centre, and bring more evidence to bear upon the part played by prostitutes in syphilitic contamination at the base.

	Syphilis contracted At the Front.	At the Base.
Free prostitutes	6	140
Landladies	—	2
Servants	2	6
Married women	—	8
Legitimate wives	—	1
Total	8	157

Hence, soldiers at the front most frequently contract syphilis in the interior, either in the depots before returning to the front, or when on leave.

Men on leave have various opportunities of contracting venereal disease : from the moment of quitting their unit they pass through towns in the military zone where syphilis is rampant, and stop at railway and transport junctions, often in Paris, where the station approaches are seething with women of all kinds. Jolivet, out of 100 patients, cites no less than 6 cases (2 syphilis, 4 gonorrhœa) contracted from women near railway stations by men passing through the towns. I have heard authoritatively that men have even been contaminated in the train taking them on leave by women who walk the trains and succeed in escaping observation.

At the place of destination there are various sources of contagion : barmaids, waitresses, laundresses, and work-girls give themselves up to clandestine prostitution ; there is also the mistress who, abandoned on mobilisation, has since taken one or more lovers. Men

who have been mobilised longest sometimes incriminate their wives : medical men at the front cannot verify the accuracy of the statements of their patients, and, despite the number who assert that their wives have contaminated them (16 in Jolivet's statistics, 11 in Carle's), may be sceptical. Facts observed in the interior, of women infected in the absence of their husbands, and dreading to infect them when on furlough, leave no doubt as to the reality and relatively large number of these contagions. Indeed, it has occasionally been possible to examine the husband when on subsequent leave, and make an accurate inquiry into the evolution of the two infections with syphilis. I myself have seen more than forty absolutely authentic cases.

In the *army zone,* contamination mostly emanates from women whose business brings them in contact with soldiers : restaurant keepers, barmaids, laundresses to whom the men send their washing on returning to quarters ; seamstresses, who mend their clothes, as well as farm-girls met near camp, or in the open country. Often the women are married (31 out of 113 contaminations in the army zone, according to Carle's statistics), town or country women; these latter are almost as numerous as professionals, registered or clandestine, free or in houses, mentioned in the same statistics (35 professionals as against 32 married women).

To sum up, in the army zone, venereal diseases are transmitted more often by women who are not professional prostitutes than by official or clandestine prostitutes living solely by their bodies. If one could separate the contaminations occurring in large towns and at the base from those occurring in the army zone, the part played by true prostitution in the dissemination of syphilis and venereal diseases in the immediate neighbourhood of the front would be very considerably diminished.

In the Table published by Carle a suggestive comparison may be made of venereal contaminations by professionals, according to whether these were produced in the army zone or in the interior ; in the latter they give 114 contaminations out of 178, *i.e.* 64%, and in the army zone 35 out of 113, *i.e.* 31%, or less than half.

There is, therefore, a danger to soldiers in women who are apparently most innocent, and the importance of this cannot be exaggerated. I even heard some military surgeons say that every woman in the war zone ought to be watched, and that no social position should prevent the suspicion of syphilis from being traced to its lair. Proportionally as the war is prolonged, the opportunities for these women contracting syphilis will be multiplied, with consequent increase in the dangers run by the troops.

Syphilis is very irregularly distributed in the different bodies of troops, and I could cite such and such a regiment in which the number of cases of syphilis is at the lowest, although, and perhaps because, medical inspection is made regularly and carefully. In others, on the contrary, syphilitic morbidity is high. These inequalities, for the greater part, are due to the sanitary condition of the women with whom the men have intercourse : owing to the small number of women living near the front zone, it only requires a few of them to become syphilitic for contamination to multiply with extreme rapidity. Equality amongst the different bodies of troops, in this respect, tends to re-establish itself by the movements of the men on furlough.

In the *base zone*, on the other hand, contagion originates especially with professional prostitutes who swarm in the large towns * in search of soldiers quartered

* L. Spillmann (" On the Increase of Syphilitic Morbidity among Troops on Active Service," *Comptes rendus de la Société de Médecine de Nancy*, December 22nd, 1915) has noted the increase in the number of prostitutes at Nancy. This has also been reported to me from all the large towns near the front.

in these towns, and with other women brought there by their duties, or passing through when on furlough. For some time there has not been one of these large towns in which syphilis has not made an incessant advance ; statistics are wanting as to the sanitary condition of these towns, but the declarations of both civil and military surgeons, and the afflux of syphilitic women into the hospitals, prove it abundantly. It is in these towns that the most rigorous supervision of both official and clandestine prostitution should be exercised.

The risks of contamination in the base zone explain why syphilis is extremely frequent amongst men staying there, or who have easy access ; such, for example, as the staffs of aviation camps, motor-drivers, secretaries of the general staff, amongst whom a high proportion of syphilitic cases have been observed by the medical men.

In the *depots* and sedentary services, the sources of contamination are similar to those noted with men on leave. They are, as in times of peace, but in higher degree, prostitutes of all kinds. Statistics of my clinic show that, out of 31 syphilitic soldiers, 20 had been contaminated by avowed professionals, and 3 others also probably by professionals. In these 20 contaminations it was always a case of solicitation, especially around the Paris railway-stations and near the depots. We thus come to a proportion of 64, or perhaps 70% of infections by prostitutes. Comparing, in the same statistics, the round numbers (civil and military combined) of cases observed (165) with those of the contaminations emanating from professionals (which extend certainly to 99, and probably to 122), a similar percentage is reached, which shows that 60 and probably 73% of the contaminations are due to professionals.

Meetings take place on the public highway, near the Paris railway stations, in military centres, at depots, concerts, cinemas, etc.

For men mobilised in *munition works*, the habitual source of syphilitic contagion is also the prostitute, at least in Paris. In provincial towns, it is more likely to be caught in the workshop : the promiscuity of the sexes entailed by the necessities of work, and more especially its inspection (women being inspected by foremen) facilitates more or less durable *liaisons*, with resultant contaminations. It is noteworthy that a certain number of pre-war prostitutes, whose clientele had been reduced by mobilisation enrolled themselves amongst munition workers. It has been stated that, in a large provincial town, the majority of certified prostitutes were engaged in munition work, their wages increasing the profits, reduced by war, of prostitution, which they continued to practise with their fellow-workmen.

Non-venereal contaminations occur in the Army ; the proximity of the trenches and camps, the common interchange of mugs, forks, pipes, etc., are sufficient to explain these. Cuts from the improvised barber's razor, often a poor one, may also produce syphilitic infection.

As a matter of fact, however, despite inadequate precautions, such contaminations appear to be rare in the Army.

CHAPTER III

SYPHILIS AS A NATIONAL DANGER

THERE is no exaggeration in stating that the present-day frequency of syphilitic contamination constitutes a danger of the first importance, which will have an influence upon the nation quite as considerable as that of the most deadly epidemics.* This danger can only be compared to that of tuberculosis, against which it is justifiable to take the most rigorous and expensive precautionary measures.

Before showing of what these dangers consist, the modes by which the propagation of syphilis undermines the national defence, compromises the vitality of the nation, racial vigour, and the repopulation of France, it may be well to complete the picture of syphilis in this country and to sketch rapidly its present effect on the civil population.

SYPHILIS AMONGST THE CIVIL POPULATION SINCE THE BEGINNING OF HOSTILITIES

In the preceding chapter I indicated the frequency and origin of syphilis in the Army, and the influence of the civil upon the military environment.

Like all contagious diseases, and more especially for

* This is no new danger, nor is it the result of the present war alone. Landouzy ("Syphilis before the War. Disregard of its extreme Frequency," *Bulletin de l'Académie de Médecine*. Meeting of April 18th, 1916, p. 434) has shown with great force and appropriateness that it has long been in existence, and has remained unsuspected by far too many.

the majority of them, endemic syphilis in the Army does not limit its effects to the soldiers themselves, but has an immediate and extensive repercussion upon the civil population. The conditions of syphilitic transmission explain, without further detail, this exchange, which is far too free. Let us see how this influence of a military centre affects civil life.

Here, again, available statistics are wanting. Syphilitic morbidity of different social districts in times of peace is subject to variations, difficult to disentangle from a rough accumulation of figures, and these social centres have been upset by the war. The influx of refugees has modified the population, especially the number of those attending the hospitals; the utilisation of female labour has changed the composition of workshops, causing an influx of women of restricted means, forced by the war to earn their own living. What can I say further? In the hospital clinics the proportion of syphilitic cases recently reported, among the total number in hospital, would seem to indicate an increase of syphilis; but the conditions of admission to hospital of cutaneous affections are quite different to those of peace time: refugees are sent to hospital for benign diseases which would have been treated at home; patients suffering from chronic affections have left hospital to work, etc. The result is, without counting that the diminution in number of medical students does not allow of the collection of all facts from the hospital statistics, that these statistics do not contribute elements of certainty to the study of the increase of syphilis.

It is imperative, therefore, to abide by the impressions of medical men; and all declare that syphilis has increased, not only specialists, but general practitioners as well.

Brocq * wrote in January, 1916: "I shall not, in

* Brocq, "The Influence of the Present War on Cutaneous Affections" (*Bulletin médicale*, January 22nd, 1916, p. 111).

this note, insist upon the heartrending frequency of venereal diseases, and the terrible increase in syphilis since the beginning of hostilities : my sole occupation to-day will be cutaneous affections properly so-called, and yet I cannot state too emphatically that the true aspect of our clinics during the war is dominated by the deplorable prevalence of syphilis."

A very distinguished doctor, belonging to an Accidental Insurance Company, Dr. Borne, recently informed me that, whereas before the war he rarely saw one patient a month in whom he could find a trace of venereal disease, syphilitic eruptions, mucous plaques, gonorrhœal arthritis, etc., at the present time he comes across three to four per week.

There is no doubt that, in a general way, the number of cases of recent syphilis has increased amongst the civil population since the war, and there is evidence of still further advance. I repeat, this is the result observed, from the discussions I have had with a number of medical men, all of whom have confirmed these statements.

This does not apply specially to Paris ; it has been observed by all medical men I have questioned, both in large centres and small localities.

Indeed, not only is the increase of syphilis observed in Paris and large towns ; it has also been noted in small towns and localities soon after a military influx (near the front, in training camps, especially quarters at the base, in the rest billets, depots for troops, motor and aviation centres, hospitals, etc.), and among munition workers. It is even relatively perhaps more important in small localities than in big towns, where syphilis has always been present.

There are two civil classes especially in which this augmentation has been surprising : amongst married women and young men.

All medical men at special hospitals have noted that the number of *married women* who come to

consult them for syphilitic troubles is altogether abnormal, and out of proportion to what occurred in time of peace.

I learn from Louis Spillmann that the number of married women in hospital at the Nancy free venereal clinic, which in 1914 was 5, with 1 syphilitic, had in 1916 risen to 43, with 23 syphilitics.

Of these women, some contracted syphilis from a civilian of some kind, a man recalled to the colours, or too old for military service, or from a refugee met by accident in the workshop or the street; here, there is no difference from what is seen in time of peace. Others have contracted the disease from men at the depots, munition workers, soldiers on leave or under treatment in the hospitals.

These two classes comprise women of varying morality, some of whom only had recourse to extra-conjugal relations as a means of augmenting their incomes, which had been reduced since the departure of their husbands.

By the side of these are the *women contaminated by their husbands* home on leave, or returned home after being discharged wounded. These women are undoubtedly syphilitic owing to the war, and they are numerous: not a single day passes without two or three, and sometimes more, presenting themselves at St. Louis Hospital for consultation. They are of all ages, sometimes young; a large number of them have no suspicion of what they are suffering from, and no idea of the nature of the sore throat, roseola, or alopecia for which they are seeking advice. They are ignorant of syphilis and its contagion, and, as a rule, it would never occur to them to blame their husbands; it is only on inquiry that the medical man, when hearing the history of the illness, verifying dates, and, finding when the husband came home on leave, has traced it to its source, this being confirmed later by the statement or examination of the husband.

I repeat, these facts are legion ; I myself having seen above a hundred cases.

Here, again, mention must be made of the munition workers. As I have already stated, and again repeat, an enormous proportion of these men are syphilitic, and, despite every possible advice, many of them take no care of themselves at all. The result is the frequent contamination of their wives, whether these live at a distance or have remained with their husbands. I have already seen a large number of married women whose husbands, munition workers, had infected them.

All these women, respectable mothers of families, sometimes pregnant or having been recently confined, are totally ignorant of syphilis, or of the fact that they may contaminate their *children*. On several occasions I have seen two or three children brought to me suffering from chancres transmitted to them by their mothers—this would be an exceptional occurrence in peace time, when the majority of syphilitic women treated in hospital know how to account for their illness.

Another fact which has struck all medical men is the frequency of syphilis in *young men* since the war began. There is no day in which several do not come up for consultation ; at the St. Louis Hospital, I myself never see less than two or three at each consultation, from 16 to 18 years of age. They have generally contracted the disease from some woman met in the street, the suburbs, or on the outer boulevards. There is little doubt that they have listened to her solicitations : won't they soon be soldiers, and must they not now prove their manhood ? When questioned, many of them reply, with a certain conceit, that they cannot say what day they were affected, as the occasions had been numerous. Then, again, there are a number of women on the streets, many of them " unemployed " owing to the reduction of the male population of the suburbs, and they have much to answer for in juvenile contamination.

These young syphilitics are the soldiers of to-morrow : military surgeons have reported with horror the proportion of recent cases of syphilis amongst the youths who have joined up during these last months.

The Social Consequences of Syphilis amongst Soldiers

To return to syphilis amongst soldiers.

On account of its frequency amongst soldiers and munition workers, this has become a danger :

1. Because it compels patients to submit to treatment which, during the contagious periods, cannot be carried out at the front, or while men are still engaged in munition works, because, in a word, it *diminishes* the effectives.

2. Because it *diminishes a man's value.*

3. Because, being transmissible to a patient's descendants, it *compromises the race* at an epoch when, more than ever before, it is imperative that the race should be numerous and robust.

Diminution of Effectives.—In order to reduce syphilitic propagation, whether genitally or extra-genitally, it is essential that the patient should be removed from his habitual environment—from his work or duty—as long as he is a carrier of contagion : this is a fact disputed by no one. This precaution is all the more necessary because genuinely effective treatment of syphilis is not compatible with the requirements of military duties in time of war.

Moreover, no matter how intense and active the treatment, in order to sterilise the contagious lesions, chancre or mucous plaques, a minimum of time is required, which varies according to the methods employed. Medical men, aware of the necessities of national defence, endeavour to reduce this period ; but, owing to the number of syphilitics, it represents a very appreciable time, and consequently a waste of effectives.

Further, syphilis, even at an early stage, and especially if not treated effectively at the beginning, may give rise to lesions which necessitate more or less prolonged treatment in hospital, so as to avoid contagion: jaundice, albuminuria, headache, ulcerative cutaneous lesions, etc., which form one part in the percentage of army morbidity.

It must be noted, also, that syphilis may play a part in the progress of wounds, retard their cicatrisation and osseous consolidation, and perhaps facilitate infection. From what I know of the operative results on syphilitic cases in general, and what I have seen since the outbreak of hostilities, this part seems very restricted; still, certain surgeons consider it of real importance. It must, therefore, also be included when estimating the influence of syphilis on the diminution of effectives.

Diminution of Men's Value and of the Duration of Human Life.—Syphilis, during its various periods and for a long time, causes a series of lesions and troubles which diminish the physical and intellectual power of man. This is not the place to describe, nor even to enumerate the cerebro-spinal, cardio-vascular, hepatic, renal, and osseous localisations which, while often attributed to other causes,* are none the less a part of syphilitic infection and gravely encumber statistics of morbidity and mortality.

There are no statistics in existence which enable one to estimate the reduction of human power entailed by the morbidity and mortality of syphilis. It would be necessary to take into account the loss of time and money caused by treatment; the incapacity to work due to the disease itself, and the influence it might exercise on different affections, especially infections and intercurrent intoxications.

* Letulle and Bergeron, "The Wassermann Reaction in Chronic Diseases" (*Bulletin de l'Académie de Médecine.* Meeting of February 22nd, 1916, p. 204).

As an indication, I may refer to the fact that, as regards workmen's accidents, the tribunals, when they have to appreciate the reduction of professional capacity as the result of syphilis, fix this reduction between 15 and 25%.

In order to give an idea of the relative frequency of later syphilitic manifestations, Fournier * compiled a Table giving the results of the examination of 4,000 patients who had consulted him for tertiary symptoms. The following is a résumé of this Table:

Syphilides and gummata	1,655
Lesions of genital organs	271
,, ,, the tongue and lips	304
,, ,, the pharynx and palatine arch	566
,, ,, of bones and of the nose	541
Gummata of tendons and muscles	19
Lesions of the digestive tube	21
,, ,, ,, respiratory passages	55
,, ,, ,, heart, aorta, and arteries	22
,, ,, ,, liver	9
,, ,, ,, kidney	31
,, ,, ,, testicle	245
,, ,, ,, eye	110
,, ,, ,, ear	24
Syphilis of the brain	764
Cerebro-spinal troubles	29
Syphilis of the medulla	135
Tabes	676
Neuritis and muscular atrophy	24
General paralysis	83
Ocular paralysis	120
Facial hemiplegia	23
Sundry nervous affections	13
Sundry localisations	19
	5,749

As regards syphilitic mortality, Blaschko,† drawing upon the statistics of insurance companies, comes to

* Alf. Fournier, *The Social Danger of Syphilis*. Report presented at the First International Conference for the Prophylaxis of Venereal Diseases. Brussels, 1899.

† Blaschko, "The Influence of Syphilis on the Duration of Life" (*IV. International Congress for Medical Insurance*, Berlin, 1908).

the conclusion that the deaths caused by syphilis represent 6% of the total mortality, that at least 30% of patients who have had syphilis die of this malady, and that syphilis shortens the duration of life by four years.

Audry * has proved that incomplete, contradictory, and doubtful results of syphilitic mortality are given by the statistics of insurance companies, the various statistics of mortality published and those of tertiary syphilis, and that inquiries into treatment in clinics and the impressions of syphilologists only give incomplete facts. He has, nevertheless, recognised that their comparison yields interesting results. The impression obtained is that the mortality, in round figures, of syphilis, specific and deuteropathic, approximates to 14 or 15%. It is believed that in France the mortality of syphilitic subjects regularly treated, young and sober, should not exceed 4 to 5%, whereas there can be no hesitation in multiplying this proportion tenfold for old men, drunkards, and certain decrepid individuals.

These causes of sickness and death enter but rarely into play during actual war, but their weight will be felt more severely by syphilitics during the following years, all the more heavily as fatigue, war emotions, preoccupations of all kinds, which will follow peace, facilitate the development and localise the disease on an organism, which, healthy and immune from syphilis, would have been able to resist it.

The consequence is a waste, of which it is impossible to estimate the importance. It is hoped, however, that the energetic treatment of primary syphilis will greatly diminish its proportions, although they cannot be ignored. Further, this waste, the direct consequence of war syphilis, will occur during the years in which the nation has the greatest need of the energy, the

* Ch. Audry, "Essay on the Mortality of Acquired Syphilis" (*Semaine médicale*, June 26th, 1906).

physical and intellectual vigour of its children, in order to repair the disasters caused by the war, and reconstruct the frame-work of industry, instruction, and scientific personnel.

Inauspicious Influence upon the Birth-rate and Future Generations.—It seems a commonplace remark, and yet it is one that must be repeated, that, after the war, it will be necessary for the French to produce many children: not only must the birth-rate fill up the gaps in the nation made by war, but, further, those which are the result of many years' voluntary restriction of births. The lessons taught by this war have been so cruel that a new mentality will spring up, quite opposed to the old order, as regards the procreation of children.

It is imperative that the classes 1935, 1936, and the following years should exceed in numbers the classes 1915, 1916, and, even if they cannot attempt to surpass them in heroism, then they must do so in physical vigour, so that they may have the maximum qualities of resistance and of physical and intellectual development, which will result in a high proportion of men fit for military service.

But, with the propagation of syphilis, precisely the opposite result will be obtained. What is the value of a syphilitic as a procreator? Nothing for several years. Not very much during subsequent ones; so much so that nearly all syphilologists * are of opinion that marriage should be forbidden for four years at least, no matter how intense and active † treatment may have been, or what the serum reaction may be.

Alfred Fournier ‡ for many years has made a study of the influence of syphilis upon future generations.

* Civatte, "Under what Condition can the Marriage of Syphilitics be permitted?" (General review, *Annales de dermatologie*, 1907, p. 734).

† Brocq, "The Question of the Marriage of Syphilitics" (*Bulletin médicale*, February 21st and 24th, 1914, pp. 183 and 197).

‡ A. Fournier, *Syphilitic Heredity*, Paris, 1891, p. 89.

He has based his conclusions upon 500 observations, in which he has been able to distinguish paternal heredity, maternal heredity, and mixed heredity (father and mother), and considers that these three kinds of heredity have the following influence on the morbidity and mortality of the child :

	Indications of Morbidity.	Indications of Mortality.
Exclusive paternal heredity .	37%	28%
„ maternal „ . .	84%	60%
Mixed heredity . . .	92%	68·5%

These statistics show that maternal heredity has a much greater noxious influence than paternal heredity : the contamination of a woman by her syphilitic husband may take place several years after his infection, thus pushing further back the period during which the pair can have healthy children.

The noxious influence of syphilis certainly becomes more attenuated as the years roll by ; not only do the number of abortions diminish, but the mortality of children born at term also decreases rapidly.

Alfred Fournier * has recorded the deaths of 176 children out of 239 pregnancies in syphilitic families, and has noted the date of these pregnancies in connection with maternal infection :

First year	88
Second year	34
Third year	17
Fourth year	7
Fifth year	5
Sixth year	6
Seventh year	5
Eighth year	5
Ninth year	1
Tenth year	1
Eleventh year	2

* A. Fournier, *Syphilitic Heredity*, Paris, 1891, p. 104.

Twelfth year	3
Eighteenth year	1
Twentieth year	1
Total	176

Out of 103 pregnancies, the issue of a syphilitic father and healthy mother, and in which the paternal influence was noxious, the same author has noted the manner in which the noxious effect was exercised.*

Children born alive, then immediately or soon affected by congenital syphilis	17
Children born alive, then showing symptoms of retarded congenital syphilis	2
Abortions or premature confinements of dead children	41
Children dead after varying periods (but generally after a short period), without any evident specific manifestations	43
Total	103

Bar has kindly shown me the observations made on syphilitic women confined in the Tarnier clinic from January 1st, 1915, to August 31st, 1916.

Those women are regarded as syphilitic who present active syphilitic troubles, proved syphilitic antecedents, or whose blood (mother's venous blood or from the cord) gives a positive Wassermann Reaction.

These statistics are interesting, as they enable us to appreciate the injurious effects of syphilis upon the offspring of women mostly subjected to the modern methods of treatment.

Out of a total of 118 pregnancies, the number of children living at the time the mother left the clinic after her last confinement is 40, *i.e.* 34%.

But this is taking a round number, which, in order to indicate the real influence of syphilis, should be

* A. Fournier, *Syphilitic Heredity*, p. 75.

RESULTS OF PREGNANCIES OF 53 SYPHILITIC WOMEN CONFINED IN THE TARNIER CLINIC FROM JANUARY 1ST, 1915, TO AUGUST 31ST, 1916.

	Last Pregnancy.	Previous Pregnancies.
1. *Pregnancies prior to syphilitic infection:*		
Miscarriages	3	15
Children macerated or still-born	20	18
Exencephalus	1	—
Children dead before mother left hospital	3	—
Children died within first year	—	10
Living children	15	5
2. *Pregnancies appearing after syphilitic infection:*		
Living children (certain or very probable contamination of mother during pregnancy)	9	—
Dead children (contamination of mother during pregnancy)	2	—
Living children born after series of miscarriages or still-born babies	—	11
Still-born children (albuminuria of mother before a series of miscarriages or still-births)	—	5
Condition of child not known	—	1
Total	53	65

subjected to an important correction, for a certain number of these pregnancies were anterior to the woman's contamination.

Counting all the pregnancies as such, where this anteriority is probable, we find that out of 90 pregnancies certainly posterior to the syphilis, there are 20 living children, *i.e.* 22%.

By taking an average, we come to the conclusion that 28% at the most of pregnancies of syphilitic women yield a child likely to live.

Further, it must be noticed that for children of the last pregnancy, observations cease 8 to 10 days after birth. How many are there still living at 20 years of age ?

Like time, anti-syphilitic treatment attenuates the noxious action of heredity. So, for a very long time, which is longer still if treatment has been inadequate,

or if syphilitic symptoms have a tendency to reappear, the syphilitic man begets a child unlikely to live, which will either not come to term, or will die in a few days. And, further, not only will the child not live, but, according to doctrine still under discussion, it will have an injurious effect upon the woman who bore it ; it will infect her, render her syphilitic, will be the cause of her bearing no healthy children for several years, and thus prolong the duration of sterility in the family.

But that is not all : the syphilitic man, who for years has been unable to beget living children, will for some years longer be unable to beget healthy or well-formed ones. His first child having been, vulgarly speaking, "rotten," his later ones will be, at any rate, "tainted." True, they live, but are often born prematurely, and are small and pallid-looking. At the end of some days or weeks, their syphilitic tendency is revealed, their nostrils and lips become covered with scabs and fissures, mucous plaques develop on their lips and tongues ; if breast-fed, the discharge from these lesions often causes a syphilitic chancre to develop on the nipple of the nurse, with resultant troubles of all kinds for the parents.

Later children may be born at term, and reveal syphilitic troubles neither at birth nor in the following weeks ; for some months their development may be almost normal, but later on they show signs of *retarded congenital syphilis*, so ably described by Alfred Fournier. They may be apparently healthy, with the exception of some accident which indicates their disease (gumma, exostosis, lesion of palate, testicular atrophy, etc.) ; but, as a rule, they are sickly, badly formed children, with weak bones, subject to chronic scrofulous ulcerations ; their genital organs are imperfectly developed, their cerebral functions affected in varying degrees, from intellectual debility or simple arrested development to complete imbecility with or without hydrocephalus.

Black as this description of syphilitic degeneration appears to be, it is but too true and too frequently realised.

Syphilis is one of the most dangerous enemies of the race and its preservation, as well as the preservation of its physical and intellectual qualities ; with alcoholism, and much more than tuberculosis, it deteriorates, if it does not radically inhibit, reproduction.

The disastrous influence of war syphilis will be felt throughout the whole country, not only in towns, where for a long time syphilis has been one of the causes of the decadence of the population, but also in country places, where previously it was not very prevalent. Therefore, the danger is perhaps greater in the country than in towns : for one reason, as experience has shown me, family contaminations are more frequent and numerous, owing to the ignorance and habits of the patients, and medical instructions are less regularly followed. On the other hand, the country may, so to speak, be regarded as the conservator of racial vigour ; the best military contingents, from a physical point of view, come off the land, and, after the terrible bleeding of the war, it will be more than ever necessary to safeguard its population, which is even now barely sufficient for agricultural purposes.

True, all syphilitics are not destined to die without issue, or to leave behind them offspring without value in the defence or enrichment of their country. Energetic and sufficiently prolonged anti-syphilitic treatment, combined with the attenuating action of time, will enable them to procreate living children, well developed both physically and intellectually : all medical men are acquainted with syphilitics who, after having been treated by the older methods, have been allowed to marry after a reasonable time, and whose children, born under good conditions, are at the present time serving with the colours. We have all seen—and I could cite several—the children of syphilitic parents who

showed undoubted manifestations in their early days, but, as the result of active and careful treatment, developed physically and intellectually enough to be regarded as fit for military service. There is reason to believe that the intensive treatment in use at the present day will yield even more satisfactory results.

It must be emphasised, however, that this is the lot of patients who have been well advised, carefully treated, and have regularly followed the orders of their medical attendants.

Amongst the legions of syphilitics infected since war began, it is easy to imagine that, after the cessation of hostilities, many of them, removed from the supervision of the medical man who attended them in the early stages, and seeing no further syphilitic manifestations appear—especially after intensive arsenical treatment —will consider themselves definitely cured, and take no further trouble, with subsequent inability to beget healthy children. To prove that these fears are not exaggerated, it is only necessary to see, at a hospital consultation, the carelessness of old syphilitics, the number of those seen for the first time and treated properly who never return and follow no treatment at all until some grave symptom appears. In an artisan population, and still more in a rural one, it is the exception to see syphilis properly treated ; miscarriages, as the result of carelessly tended specific disease, being the rule. Medical and administrative propaganda for regular and prolonged treatment have still much to do before erasing this culpable negligence.

Syphilitics recruited into the Army belong for the most part to men of marrying age, or who have been recently married, whose procreative faculties are in full development, and who are destined to repopulate the country. From a national point of view, it is of very little importance that a man of 50 or over should contract syphilis ; his procreative work is

done. But a man of 25 to 35 who becomes syphilitic has forfeited his reproductive power. As a rule, a man who develops syphilis between 35 and 45 is lost for reproduction; the period during which he should deny himself extending to an age when he will have no desire, or when his posterity would be altogether undesirable, the syphilitic influence being combined with that of age.

Taking into account the prolificness that will be necessary to bring the population of France back to its indispensable rate on the one hand, and the varied ages of the men who contract syphilis in the Army and in munition works on the other hand, there is no exaggeration in estimating that each syphilitic infection of a mobilised man will be the means of depriving France of at least one soldier and one mother of a family during the decennial period 1936 to 1945.

Pautrier expresses the same idea in the report, which I have already quoted, on the organisation of military venereal hospitals, when he says, after having attempted to specify the exact number of cases of syphilis in the Army:

"If one accepts the mean figure of 200,000, which, while hypothetical, is quite possible, and attributes to each of these cases the production of two miscarriages only, it is evident that treponemic infection will cost us 400,000 births, *i.e.* the equivalent of two classes.

"Thus, the word 'national peril' is not too strong."

Surely this consideration is of a nature to justify the most energetic measures, even the most drastic, to prevent the propagation of syphilis.

And now, when on all sides voices are being raised in denunciation of the peril of depopulation and demanding the repopulation of France, when leagues and associations are being proposed with the object of encouraging large families and protecting the life and health of children, is it not urgent to dry up the source of such a waste of life?

All that is done to protect the Army from syphilis will necessarily rebound favourably on the population.

In the following chapters I shall show how, from the military side, most rational measures have been taken under the inspiration of Medical Inspector General Vaillard. Mr. Justin Godart, Under-Secretary of State of the Health Service of the War Office, in prescribing these measures and attacking what he also, in his circular of January 5th, 1916, has called a national peril, has engaged in a more active struggle against syphilis than any minister has ever done before, and by the instructions issued on September 25th, 1916, has responded to the recommendations of the Academy of Medicine at the meeting of June 13th, 1916.

CHAPTER IV

SYMPTOMS AND DIAGNOSIS OF THE SYPHILITIC LESIONS MOST COMMONLY OBSERVED IN THE ARMY

THIS book is not a treatise on syphilis, nor is this the place to give a complete description of its various manifestations. Nevertheless, it seems advisable to refer, with necessary details, to the characteristics and diagnostic elements of the main syphilitic lesions likely to be observed amongst soldiers, especially primary and secondary symptoms. Owing to their frequency in the Army, and of their contagiousness, the military surgeon ought to be acquainted with their diagnosis.

SYPHILITIC CHANCRE

Developed at the site of inoculation of the syphilitic virus, the infective chancre in soldiers is nearly always found on the genital organs or in their immediate neighbourhood. More rarely, it is situated on the tongue, lips or tonsils, but it is then the result of accidental and not venereal contamination. It is quite exceptional for it to be found on the limbs.

After having cited the symptoms and explained the diagnosis of syphilitic chancre on the genital organs, I shall give a description of the extra-genital localisations of chancre most frequently observed.

Period of Incubation of the Chancre. Its Duration. —Syphilitic chancre—this is a characteristic of the utmost importance from the point of view of its diag-

nosis from simple chancre—does not appear immediately after the infective contact, but is separated from it by a very clearly defined period of incubation. The duration of this period is from 25 to 30 days, according to proved clinical observations, the confirmation of the patients and those who have infected them, and the experimental inoculations made on man; it is rarely less than 14 to 17 days; but may extend to 40 days, and very exceptionally even beyond that period.

Owing to the conditions of military service, especially at the front, it is often possible for the man to fix the date of the infective intercourse, when he is willing to do so. Thus, by means of careful questions, and having regard to the intelligence of the man and the conditions which may influence the veracity of his statements, it is possible to make a presumptive diagnosis from the duration of the incubation. On the other hand, comparison of the age of a chancre with the dates of leave may sometimes show the inexactitude of his statements.

In order to make use, for diagnostic purposes, of the information supplied by the soldier suffering from a chancre, it is necessary to weigh his statements very carefully, and check them in every way possible.

Causes of Localisation of the Chancre.—Syphilitic inoculation takes place through a solution in continuity of the integument, a traumatic excoriation at the moment of infective intercourse, a lesion from scratching induced by the presence of pediculosis pubis or scabies, etc. At the moment the chancre appears this lesion has nearly always disappeared, leaving no trace, and often even no recollection of it. The concomitant lesions of itch or the presence of crab-lice may still be in existence and explain certain particularities of the syphilitic infection: this is why chancres following itch are often multiple, and sometimes very numerous, the points of entry

made by the acarus being also multiple. This also explains why chancres which have appeared on persons affected with pediculi are frequently situated on excoriations due to scratching in the pubic region, inside the thighs and scrotum, regions on which a syphilitic chancre is localised more rarely than on the penis.

Commencement of the Chancre.—A chancre develops in healthy skin ; it commences as a rounded papule, bleeding easily, of firm consistency, with a slight erosion in the centre ; but at this stage it has no pathognomonic characteristic. It must be added, further, that the chancre is rarely observed by the medical man at this stage, and indeed can only be noticed in patients who are scrupulously careful or nervous, who consult a doctor the moment there is anything abnormal on their genital organs.

During the following days the lesion progresses, becomes larger and more defined, the induration increases, and the ulceration extends.

Stage of Maturity.—When the syphilitic chancre has developed it is possible to define it as an ulceration situated upon a hard base. I ought rather to say ex-ulceration, for the loss of substance is very often superficial.

Smooth, with a regular surface, presenting neither depressions nor projections, such as are seen on the irregular base of simple chancre, the ex-ulceration is ordinarily on a level with the neighbouring skin, sometimes it projects above it ; occasionally it is depressed and saucer-shaped ; more rarely still, it is excavated.

The surface of this ulceration is generally glazed of a special red colour, which has been compared by all classical writers to that of muscular tissue ; if observed carefully under a magnifying glass, it is found that it is not uniform, but very finely granulated, sprinkled with little specks of deeper red, which are

nothing but fine vascular dilatations. Some chancres are of a different colour ; they are covered by a greyish layer, almost diphtheroid, which, although not thick, is very adherent. This coloration often does not cover the whole surface of the chancre, but forms a concentric circle around its border ; the result is a peculiar appearance, which goes by the description *chancre in rosette.*

Syphilitic chancre of the genital organs does not suppurate ; here it differs completely from simple chancre : all it does is to exude a very small quantity of serous fluid, which keeps up a slight moisture on the surface and aids in giving it its glazed appearance. J. Nicolas * has called attention to the facility with which this discharge can be induced. It is only necessary, when the chancre has come to a head, to execute slight friction with a hard body such as a platinum spatula or vaccination needle, to see the surface covered over by a clear, transparent serum : this discharge, if the friction is continued, becomes abundant enough to be collected with the spatula or needle.

This characteristic is very important from the point of view of diagnosis of the chancre, because it is in this exudation resulting from serous drainage of the superficial layers of the chancre that it is most easy to detect the presence of the spirochæte. I shall refer again later to this point, when discussing the bacteriological diagnosis of chancre.

On the skin, or more accurately in the regions where the nature of the integument does not allow of a certain degree of constant moisture, the secretion of the chancre forms into more or less thick scabs (*scabous chancre*) ; but these scabs always remain dry, and no layer of pus is found below them, such as happens with simple chancre or with ecthyma.

* J. Nicolas, " Schaudinn and Hoffmann's Spirochæta Pallida and Syphilis" (*Lyon médical*, October 1st, 1905, p. 497).

Syphilitic chancre is nearly always of regular formation, extremely regular, geometrical, rounded or oval. In certain regions, like the anus, it may take on a fissure-like form, or be disposed like *the leaves of a book.*

The dimensions are variable. It may remain small through its whole evolution, in a state of *dwarf chancre*, resembling a herpetic erosion. The average size is about the size of a sixpence. It is altogether exceptional, especially on the genital organs, for it to attain the size of a shilling or over : it is only on the body that larger dimensions may be attained, meriting the name of *giant chancre.*

The ulceration of a syphilitic chancre rests upon an *indurated base* ; this is the main characteristic, which is of great importance from a diagnostic point of view, and has gained for it the name of indurated chancre. As a matter of fact, it is altogether exceptional for the induration to be absent, especially in man ; but it varies in intensity.

In order to appreciate this clearly, it is necessary to proceed methodically : the thumb and index finger, covered by a rubber finger-stall, or protected by lint,* and opposite to each other, are placed one at each of the extremities of one of the diameters of the ulceration and at a centimetre or demi-centimetre outside it ; approaching one to the other, the base of the chancre is slightly raised by means of moderate

* It cannot be urged too strongly on medical men to take precautions, when called upon to examine patients suffering from ulcerous lesions of the genital organs or other regions. They should, first of all, see that there is neither sore nor excoriation on any of the parts likely to come in contact with the suppurating lesions of their patients, and, if they have any, these should be covered up with plaster.

At a consultation, at which a certain number of venereal patients are present, it is a good thing to have rubber finger-stalls at hand, which should be put on before manipulating the chancres.

A compress, or even a thin tuft of wadding, can be used instead of gloves.

After touching an ulceration, the doctor should wash his hands

pressure ; it is then easy to feel, between the two fingers, the existence of a firm plaque of regular consistency, but varying in one case from another. It is more like the sensation that would be given by a sheet of thick paper or parchment (papyraceous induration), rather than that of cartilage, or even of a piece of wood (ligneous induration). There is always a certain elasticity in this induration. Unless it is very large, it can be distorted slightly by pressure, and the surface of the chancre, from being level, becomes slightly convex, like a sheet of flexible cardboard.

The degree of induration is often, but not always, in relation to the dimensions of the chancre : dwarf chancres may have a very indurated base, voluminous chancres may rest upon a papyraceous induration.

The induration always extends beyond the limits of the ulceration. When it has reached a certain degree it forms, as it were, a pastille with an ulcerated centre.

The induration of some chancres is obvious : situated upon convex or cylindrical parts, they do not conform to the contour, but their two extremities project from the adjacent tissues, thus proving that their base is hard and unyielding. The induration gives rise to a particularly curious phenomenon in chancres occupying the internal surface of the prepuce near its insertion : if the prepuce is retracted, at the moment its folds reach the lower border of the chancre,

with soap and water, or, simpler still, dip the fingers into alcohol, as they may have been soiled by the secretions.

Further, I cannot recommend too strongly that the genital organs of a patient should never be examined without having exposed the entire region, and ordered the patient to remove his hands : these, which have often touched the dressings or ulcerations, may be soiled by contagious pus, and the doctor risks contamination from the scratch of a finger-nail, should the patient move suddenly.

Finally, the medical man should always see that the dressings which have been in contact with the ulcerations are not, under any pretext, placed on a chair or on the floor, but are put by the patient himself into a receptacle, or on a paper to be burned.

it is lifted abruptly on to the corona of the glans, executing exactly the same movement as the tarsal cartilage does during the eversion of the eyelid. In these cases, it is almost unnecessary to feel the induration with the fingers : it reveals itself to sight, and cannot be mistaken for anything else.

Besides the induration, the base of a syphilitic chancre may be the seat of more or less pronounced infiltration and of tumefaction, which cause considerable deformity. Thus certain chancres of the prepuce produce very marked phimosis, with enormous increase in the volume of the prepuce, giving rise to distortion, described as " bell-clapper penis," which is almost pathognomic of syphilitic chancre. Through the œdematous and tumified prepuce, it is possible to feel one or more indurated plaques, indicative of chancres of the prepuce concealed by the intensity of the phimosis.

Contrary to simple chancre, the syphilitic chancre is painless, spontaneously, under the influence of pressure, or of exterior contact. Nevertheless, chancres situated on the preputial orifice, or on the urinary meatus, are painful during micturition. External irritation may occasionally render chancres painful, no matter where situated, by inducing inflammation.

Habitual Unicity of Syphilitic Chancre ; its Frequent Multiplicity.—Although a syphilitic chancre is generally single, this is not the case as much as is currently believed from the schedule of Ricord. It is multiple in one case out of four ; but it is rare to observe more than three or four in the same subject. Multiple chancres may be situated on the same region, or on different parts of the body : in this way, one may see a chancre of the genital organs and one of the anus or cephalic extremity developing simultaneously, according to the hazards of inoculation.

Results of the Inoculation of Syphilitic Chancre on the Bearer of the Chancre.—It has long been considered an important characteristic of syphilitic chancre that it

was impossible for it to inoculate its bearer. The researches of Queyrat have recently shown that, under this form, the proposition was not correct, and that, at any rate during the first weeks of its evolution, it was possible to obtain a lesion of a chancrous nature at the point of an inoculation ; this lesion becomes more and more attenuated, in proportion to the age of the chancre, but is always characterised by more or less pronounced induration, with or without ulceration.

The old opinion, therefore, cannot be regarded as strictly accurate. It is none the less true that the syphilitic chancre differs from simple chancre, from the point of view of inoculation. Whereas the latter, up to an advanced period of its evolution, reproduces by inoculation a lesion at the end of about forty-eight hours, characterised by a pustule and leading on the fourth day to the development of a deep ulceration with detached borders, inoculation of the secretion or tissue of a syphilitic chancre produces nothing in this time, and gives rise, after ten to fifteen days, to a lesion characterised by an infiltrative papule which may afterwards become ulcerated, but never becomes an ulcer with detached borders. In short, inoculation of the infecting chancre never gives rise to the inoculation lesion made known by Hunter and Ricord ; the law of Bassereau remains always true.

Evolution of the Syphilitic Chancre.—When left to itself, the syphilitic chancre lasts about four weeks ; parchment-like chancres evolve more rapidly, while extensive ones with much induration last longer. Treatment, especially with arsenobenzol, hastens the cicatrisation of the chancre.

Healing is evidenced by diminished induration ; the diphtheroid membrane, if it existed, falls ; the surface becomes less red, granulates, and heals up ; the ulcer gradually contracts.

After healing, a level, soft cicatrix remains, which is pigmented for a long time and often retains a certain

degree of infiltration and induration appreciable to careful palpation for several weeks, especially if the chancre has not been treated with arsenobenzol.

Effect of the Chancre on the Vessels and Lymphatic Glands (*Lymphitis and Adenopathy*).—The syphilitic chancre rapidly implicates the vessels and lymphatic glands, more than any other cutaneous or mucous lesion.

A few hours after its appearance, it is frequently accompanied by *lymphitis* ; this is specially appreciable with chancres of the prepuce and glans, on the dorsal surface of the penis, in the form of one or two slightly moniliform or smooth indurated cords, which have often been taken for phlebitis. This lymphitis persists for the duration of the chancre, and disappears at the moment of its cicatrisation.

The lymphatic glands corresponding to the region of the chancre are also affected at an early date. The *satellite adenopathy* of the chancre, which, at first single, rapidly becomes multiglandular ; hard, enlarged, isolated from each other, the glands are painless on pressure, and movement. Sometimes, however, under the influence of traumatic irritation and secondary infection, they may become inflamed, increase still further in volume, become surrounded by periadenitis, and painful, but they practically never suppurate.

According to Ricord, a more voluminous gland is often seen in the midst of smaller ones, which is sometimes harder and corresponds, according to classical teaching, to the lymphatics coming directly from the chancre.

The adenopathy of a syphilitic chancre, however, is not always in direct anatomical relationship with the seat of the chancre itself ; it is not unusual, with a chancre clearly on one side of the glans or prepuce, to see adenopathy develop in both groins ; nor, with a chancre similarly situated, to find the lymphatic glands on the same side immune, whereas those

on the opposite one are the seat of very pronounced adenopathy.

It is well to note that, in exceptional cases, the regional adenopathy is absent during the whole of the evolution of the chancre.

The adenopathy persists after the chancre for some weeks, often for months ; it disappears more rapidly with patients who have been treated with arsenical preparations.

Diagnostic Elements of Syphilitic Chancre

The diagnosis of syphilitic chancre depends on four factors : the objective signs ; its evolution ; signs drawn from the patient's antecedents and the appearance of symptoms of secondary syphilis ; lastly on laboratory researches.

Diagnostic Importance of the Objective Signs

Of all the objective signs already described, the most important are : the slight depth of the ulceration ; absence of detachment of the borders, this sign enabling one to recognise that it is not a question of simple chancre ; induration of the base.

This last characteristic is of the utmost importance : a clearly defined induration, limited to the base of the syphilitic chancre, is almost a pathognomonic sign. But it is also necessary that the *induration* belongs to the lesion it accompanies, and is not superimposed.

It often happens that a simple ulceration, an excoriation occurring during coitus, herpetic ulceration, etc., has been subjected to irritant treatment, covered with unsuitable remedies, and has become surrounded by an inflammatory inflammation simulating the characteristics of basal induration.

Various remedies, sometimes the most improbable ones, may cause this condition. It is frequently noticed after the application of ashes from a pipe, a

very favourite remedy among the people. Some patients, haunted by the fear of syphilis, directly they notice an ulceration of the genital organs, hasten to heap upon it all the antiseptic liquids they have to hand : tincture of iodine, concentrated carbolic acid, permanganate of potash, peroxide of hydrogen, sublimate, nitrate of silver, etc., and to cover it with all the powders of the pharmacopœia. The result is that, when they consult a doctor, it is impossible for him to diagnose the cause of the induration, which might equally well belong to the lesion itself, or be the consequence of unsuitable treatment.

A much more frequent cause of induration is the use of calomel on ulcerations of the genital organs, either in the form of powder or of ointment. These two remedies have for long been advised by famous syphilologists in the treatment of syphilitic chancre : experience has long shown, however, that they are of no special value, and should be abandoned. But, above all, they must *never*, *under any pretext whatever*, be applied to an ulceration not yet properly diagnosed.

Under these conditions, *calomel, either as powder or ointment, must be prohibited in the treatment of ulcerations of the genital organs.*

Inflammatory infiltration differs from true induration by having less firmness, less regularity, and less clearly defined limitation. When the infiltrated base of a simple ulceration is pressed between two fingers, this base can be depressed and modelled, so to speak, instead of becoming tense, and raised with a certain convexity, like the syphilitic chancre ; when pressed on the two extremities of one of its diameters, its surface seems to double up under the fingers. If doubt still persists after examination and the other diagnostic elements are uncertain, the patient should be told to apply a dressing of boiled water for two or three days to the exclusion of any other remedy : an inflammatory infiltration generally becomes modified or disappears

at the end of this time, whereas a syphilitic chancre persists.

Diagnostic Value of the Signs drawn from the Evolution of the Chancre

I have already indicated (see page 34) the existence and duration of the incubation period of syphilis. It is necessary to revert to this here, in order to show that, in certain cases, this factor is of great importance in diagnosis. A simple chancre has no incubation, or at least the period is very short, not exceeding two or three days; so that, in every case where an ulceration develops more than four or five days after the last coitus, the diagnosis of simple chancre is untenable.

On the other hand, the fact of recent coitus is not sufficient to eliminate the possibility of syphilitic chancre, contamination possibly extending to an earlier one. It is only in the case where, the patient's statements appearing to be perfectly truthful, no possibility of syphilitic infection can be found for several months, apart from the recent coitus, that, relying on these statements alone, one might admit with certainty the existence of a simple chancre.

Deductions drawn from the statements of the patient, as I have already remarked, have but a relative value, depending on his truthfulness and intelligence.

Signs drawn from the Patient's Antecedents, or from the Appearance of Symptoms of Secondary Syphilis

Syphilis only recurs exceptionally; the certain knowledge of previous syphilis should put one on one's guard against the diagnosis of syphilitic chancre. To tell the truth, it is a dangerous postulate to reject this diagnosis, for the sole reason that the patient states he has previously had syphilis or a chancre. In the first place, the patient's statements may be incorrect, con-

fusion existing in his mind between all venereal diseases : what he had previously called syphilis may have been nothing but gonorrhœa, an error which can be overcome by making the patient specify the symptoms he has experienced.

In the second place, the diagnosis of the first affection may have been incorrectly made by the practitioner consulted at that time, a mistake more difficult to eliminate.

Finally, rare as they are, syphilitic re-infections do take place, contrary to the opinion of Ricord and Alfred Fournier; but these must not be admitted unless the diagnosis of the first attack, and that of the second, are based on undoubted facts.

Thus, if in a patient the antecedents of former acquired syphilis seem certain, it will be necessary, before diagnosing infective chancre, to be doubly sure and to have this confirmed by the most accurate methods—I am not now speaking of hereditary syphilis, or at least of hereditary antecedents of syphilis, for it is demonstrated by numerous observations that the descendants of syphilitics may contract the disease like others.

The development of secondary syphilitic affections appears, under normal conditions, after an ulceration which has presented more or less marked characteristics of syphilitic chancre, and may help in the diagnosis of the latter. We shall see, as a matter of fact, after having recourse to all methods of examination, that a doubt may still persist as to the nature of a genital ulceration : this can only be determined by the appearance of roseola or of mucous plaques. But, as secondary symptoms only develop six weeks after the appearance of the chancre, this is the slowest method to which one can have recourse, a final one, a makeshift one for which one would only decide to wait under very exceptional and specially embarrassing circumstances.

Indications supplied by Laboratory Researches

Experimental bacteriological researches, since 1905, have brought an aid to syphilitic diagnosis, which cannot to-day be ignored in doubtful cases.

Without discussing the laboratory inoculations of animals, which in certain limited cases may render first-class help, but are totally impracticable in the laboratories improvised in sanitary centres, there are two methods which can be utilised for general syphilitic diagnosis : research for the parasite of syphilis and complement-fixation.

Research for the Parasite of Syphilis.—The spirochæte of Schaudinn and Hoffmann, to-day generally called *Treponema pallidum* in France, if definitely found, is sufficient to classify as syphilitic the lesion in which it has been demonstrated, and if this lesion presents the objective or evolutionary characteristics of a chancre, it can be stated definitely that it is a syphilitic chancre.

It is easy to look for this parasite : it can be done with any microscope, with the aid of staining methods, if the microscope used is only an ordinary one, or by direct examination of the preparations on a dark field, if the observer possesses a so-called ultramicroscope.

The first rule to be observed, in searching for this parasite, is to examine the preparations in which it is possible to find it, if it is present.

Indeed, infective suppurating chancres supply secretions full of microbes of all kinds, in the midst of which the spirochæte is unperceived, or confused with the innumerable series of non-pathogenic spirillæ.

Further, the various antiseptic remedies used wrongly or rightly in the treatment of ulcerations of the genital organs have the effect of destroying this very vulnerable parasite, at any rate in the superficial layers of the ulceration.

Hence, if the treponema is to be searched for in an ulcer of the genital organs, whether suppurative, infective, or treated by some antiseptic, it is necessary to put a dressing of boiled water only on the ulcer for at least forty-eight hours, which should be kept on permanently and renewed twice daily, and bathe it also with pure boiled water; every antiseptic, no matter how weak, being absolutely excluded.

Chancres covered with a diphtheroid layer should also be subjected for forty-eight hours to dressings of boiled water.

To collect the material for examination : the best method consists in applying superficial friction to the surface of the ulcer, by means of a hard body, a platinum spatula or vaccination needle, which should be first sterilised by heating in a flame. The ulcer will soon be covered by an abundant serum.

Nevertheless, in chancres of long standing this serum is only obtained with difficulty, and not in adequate quantities for examination purposes ; it is necessary to scarify the surface lightly and collect the mixture of blood and serum which flows from the scarifications.

The fluid is spread on a slide in a thin layer. If the examination is to be made with an ultra-microscope it is simply covered with a cover-glass and examined direct. In the absence of the ultra-microscope, recourse must be had to staining methods.

The classical method of microscopic examination of the spirochæte is that of Giemsa, which has the advantage of supplying a fairly characteristic coloured reaction. This method consists in diluting Giemsa's solution (which is composed of 3 grammes of Azur II Eosin, 0·8 gramme of Azur II in 250 grammes of glycerine, evaporated to dryness, and added to 250 grammes of Methyl Alcohol in the proportion of 1 drop to 1 cubic centimetre of distilled water. The preparation is dried in air, then fixed for ten minutes

in absolute alcohol, or it may be fixed, before drying, by osmic acid vapour ; it is then immersed for one or more hours in the colouring solution. For a rapid diagnosis, the same solution may be used, rather more concentrated and with, or without, the addition of ½% glycerine ; staining is then produced by heating until steam is produced, renewing the fluid 3 to 5 times ; staining is complete as soon as the blood-corpuscles appear vividly pink under a low magnification.

With Giemsa's method of preparation, the microbes are coloured bluish-violet, as well as the non-pathogenic spirilla and the cell nuclei, the blood-corpuscles are pink, and the treponema pallidum reddish-pink. It is seen best in the neighbourhood of the blood-corpuscles.

In default of Giemsa's * reagent, one can have recourse to silver staining, already made by Ravaut with largine, and which Fontana carries out in the following manner : the preparation is fixed and decolorised, by means of an aqueous solution of acetic acid (1%) and of formol (2%), then heated for 30 seconds in a 5% solution of tannic acid, and, after washing, treated with an ammoniacal solution of 5% nitrate of silver, also for 30 seconds.

The Chinese ink method has been employed more abroad than in France. Owing to the facility of its use, and in default of an ultra-microscope, it may be of service in army laboratories. It consists in the employment of a dilution of Chinese ink, which forms a dark ground on which the treponemas appear colourless.

As a general rule, however, the favourite method of seeking for the spirochæte is examination on a dark ground, called the *ultra-microscope* method. I think it has been adopted by all syphilologists, on

* Giemsa's solution, being the monopoly of a German firm before the present war, is now being prepared by French manufacturers.

account of its rapidity and simplicity; but it necessitates special apparatus, which is not provided in many of the army laboratories and medical centres. With the illumination obtained from this apparatus, the ground-work of the preparation remains dark, whereas the corpuscles immersed therein are vividly illuminated and show up very clearly.

The examination is made either with a dry or an oil-immersion lens, in fresh preparations, in which the spirochætes are seen living, moving from place to place, thus facilitating research and their identification.

In fixed and stained preparations, the spirochæte appears as an extremely fine thread, tapering at its two extremities and twisted into a spiral like a corkscrew, with many turns (6 to 12 on an average). The turns of the spiral are narrow, regular, and deep. The total length of the parasite is from 5 to 20 μ; its width from $\frac{1}{4}$ to $\frac{1}{2}$ μ; on an average its length slightly exceeds the diameter of a blood corpuscle.

Examined with the ultra-microscope, it is mobile. It can move round its longitudinal axis, advancing or retreating by jerks and in a straight line; or, while remaining in the same place, it performs undulations or makes movements of flexion and torsion; sometimes its two extremities unite so as to form a circle.

The Treponema pallidum is distinguished from other spirilla by its regularity, the multiplicity and permanence of its spirals, its mobility in the living state, and its reaction to staining media.

The *Spirochæta refringens*, which frequently exists on the surface of ulcerous lesions of the genital organs, and with which it might be confused, has not so many spirals. These are irregular, very elongated, and not deep; it changes but little under the influence of reagents or in its movements; it is thicker than the treponema, and is deeply stained by the usual stains.

In ulcerations of the mouth, and even of the lips,

there is a possibility of confusion with other micro-organisms, difficult to avoid, even by an expert observer. The greatest precautions must be taken, therefore, when the diagnosis of syphilitic chancre of the mouth has to be determined by bacteriological examination. The following is a list of the special characteristics of buccal spirilla, which might be confused with the Treponema pallidum.

The *Spirillum dentium* is like the treponema as regards its slimness and the regularity of its spirals, but differs as to length (4 to 10 μ at the maximum), and especially in the slighter depth of its undulations.

The *Spirochæta buccalis* is, on the other hand, easy to recognise on account of its great length, its thickness, the irregularity of its spirals, and its extreme mobility.

Vincent's Spirillum is longer and thicker than the Treponema pallidum, its spirals are irregular and not deep ; it is associated with the fusiform bacillus.

The *Spirochæta refringens* is almost the only spirillum which may be confounded with the Treponema pallidum in the scrapings obtained from ulcerations of the genital organs.

The presence of the treponema in the scrapings of an ulceration of chancrous appearance enables one to prove that this ulceration is a syphilitic chancre ; but its absence would not definitely exclude such a diagnosis.

Indeed, it is by no means exceptional for it to be absent in undoubted cases of chancre.

In the first place, it may have been dispersed by the use of antiseptics, to which it is very sensitive. Secondly, the surface of the ulceration may be the seat of various secondary infections, the pathogenic agents of which have caused the treponema to disappear, or prevented the verification of its presence in the scrapings. I have already shown that these two causes of error might be prevented by using

dressings and bathings of boiled water for forty-eight hours.

Finally, there are chancres in the scrapings of which it is impossible to distinguish the presence of the treponema, no matter what care is taken. These chancres are nearly always of long standing, extending beyond fifteen or twenty days, in which the tissue is more or less sclerosed, the scrapings yielding but the slightest exudation, and in which even deep scarifications do not succeed in reaching the foci of treponemæ.

In these cases it would be possible to obtain evidence of the treponema from sections of the chancre, hardened in alcohol and impregnated with silver after Bertarelli's method ; but it would be necessary to make a partial excision of the chancre, and the patients might refuse to submit to this ; further, this method of examination can only be accomplished in a well-appointed laboratory. It could not, therefore, be recommended in army practice.

Researches for the Fixation of the Complement (Wassermann Reaction).—Many medical men believe that the complement-fixation test, by means of the method of Bordet and Gengou called the Wassermann Reaction, is of the highest importance in the diagnosis of syphilitic chancre. Every day soldiers are sent to the bacteriological laboratories with a note, containing the following statement : " Probable syphilitic chancre; kindly make a Wassermann Reaction."

This belief is wrong, and if one relied upon the result of the Wassermann Reaction for determining the diagnosis of chancre, it would be erroneous nine times out of ten.

The views of medical men in general, and even of experts in the Wassermann Reaction, are very vague, as I have taken the opportunity of finding out, and, in plain words, absolutely false. Many medical men practically believe that, on the one hand, the existence

of this reaction is sufficient to establish the syphilitic nature of any lesion borne by the patient who has supplied the serum examined, and, on the other hand, the absence of this reaction is sufficient to prove that the same lesion is not syphilitic.

Without speaking of the intrinsic value of a Wassermann test, which depends upon the competence of the biologist who made it,* and with the quality of the antigen provided, it has been definitely established that this reaction does not appear at the same time as the chancre. It does not become positive until the end of a certain time and, when it is positive, the characteristics of the chancre are, as a rule, so clear that it brings no support to the diagnosis.

Blumenthal's statistics, which are already old, will give some idea of the variations of the frequency of the Wassermann Reaction, in accordance with the age of the chancre.

Infections dating from	Number of cases studied.	Positive Reactions.	Negative Reactions.	Proportion per 100 of the Positive Reactions.
3 weeks . . .	11	1	10	9 per 100
4 ,, . . .	17	2	15	11 ,, ,,
5 ,, . . .	13	6	7	46 ,, ,,
6 ,, . . .	23	12	11	52 ,, ,,
7 ,, . . .	16	11	5	68 ,, ,,
8 ,, . . .	13	8	5	61 ,, ,,

* The Wassermann Reaction is in no way comparable to present chemical reactions: the substances used for the examination (antigen, complement) are of variable composition, and absolutely unknown dosage; the results themselves, *i.e.* the production or not of hæmolysis, are often difficult to read and appreciate.

Further, it is not rare, with the same serum, to see one observer obtain a negative, and another a positive, reaction; sometimes, indeed, the same observer will obtain a positive reaction one day and, a few days later, a negative one.

It must be added that the different methods employed for the performance of this reaction give results very different from each other.

Under these conditions, in estimating the reliance to be placed on a reaction, not only must one know the technique followed, but also by whom the examination was made.

These statistics show that it is only in the fifth week that the proportion of positive reactions is high enough for the results to be of any diagnostic importance in doubtful cases; and at this period there is not long to wait before secondary symptoms appear. Even in the eighth week there are only two chances out of three of obtaining a positive reaction.

According to the researches of Jeanselme and Vernes, the intensity of the Wassermann Reaction grows progressively during the course of the evolution of the syphilitic chancre. Comparison of the coloration obtained in several successive Wassermann Reactions might furnish an important element in the diagnosis of chancre.

Unfortunately, these comparative colorimetric tests presuppose, at the same time, the use of an antigen of exact dosage and absolute constancy, with great expertness and constant experience of the Wassermann Reaction on the part of the operator. Even in civil practice, in times of peace, they are so difficult that I do not believe they have been followed up by any other observer.

A last reflection on the value of the Wassermann Reaction in diagnosing syphilitic chancre. Being produced with the serum of old syphilitics, this reaction occurs when they are affected by tertiary ulcerous syphilides of the genital organs, which simulate the chancre and have merited the name of chancriform syphilides. But chancriform syphilides admit of neither the same prognosis nor the same treatment, nor the same prophylactic measures of isolation as syphilitic chancre. One sees to what an error a medical man would expose himself in the presence of such lesions if he relied solely upon the Wassermann Reaction, without interpreting it by means of clinical indications and the patient's previous history.

Therefore, interesting as this reaction is for the diagnosis of secondary syphilitic lesions, and more

especially of tertiary ones, it has but few applications in the diagnosis of syphilitic chancre.

Differential Diagnosis of Syphilitic Chancre

The affections most often confused with syphilitic chancre of the genital organs are: genital herpes, simple chancre, ecthyma, scabies, traumatic ulcerations, balanitis, gangrene of the genital organs, ulcerations caused for the purpose of simulation, epithelioma of the penis, secondary and tertiary syphilides, and certain ulcerations which appear after arsenical treatment of syphilis.

Genital Herpes is characterised by circular ulcerations generally covered by a whitish coating, isolated from each other, frequently multiple, with polycyclic contours. These ulcerations are deeper than those of syphilitic chancre and have been preceded by fine transparent ephemeral vesicles, which the patients sometimes remember, but not always. The lesions appear in successive crops, and in some cases it is possible to find intact vesicles near the ulcerations. The irritation caused by dirty dressings may induce a certain amount of basal infiltration, which may simulate the induration of syphilitic chancre, but it is softer, and not so circumscribed as in the chancre.

The lymphatic glands, despite what Ricord and Fournier have said, are influenced by genital herpes; but the adenitis accompanying it, unlike that of a syphilitic chancre, is slight and painful on pressure and nearly always limited to one gland.

The course of the two affections is different: herpetic ulceration heals rapidly. In a few days, in regions in which there is no moisture, such as the penis, it is replaced by a dry scab, which becomes detached and leaves a simple macule, which disappears in fifteen to twenty days, without apparent cicatrix. In moist regions it gradually shrinks up, its borders disappear,

and for some days it remains a simple reddish spot, then disappears without leaving any trace.

Under the name of herpetiform chancres, a variety of syphilitic chancres have been described, characterised by their small dimensions and multiplicity; but, no matter how small they are, they are always more extensive than herpetic ulcerations, and without their polycyclic contours.

Genital herpes is essentially a recurrent affection: its outbreaks, sometimes accompanied by pain in the course of the nerves of the genital organs, or of the thigh (Mauriac's neuralgic herpes), recur at varied intervals. The fact of relapse is important for diagnostic purposes. Nevertheless, one must not rely on the existence of numerous previous attacks of herpes for eliminating syphilitic chancre; the more so, as the syphilitic virus may be inoculated in the herpetic erosions.

A first attack of herpes, occurring in a young man, and especially in one of thirty to thirty-five, no matter how characteristic it may be, must cause reserve as to the possibility of the later appearance of chancre. As a matter of fact, syphilitic chancre is sometimes seen to develop after and in the same place as a group of herpes (prechancrous herpes). Therefore, it is indispensable, in the case of a first attack of herpes, to keep the patient under observation during fifteen to twenty days.

Simple Chancre differs from syphilitic chancre in its irregular configuration and irregular surface, by the pus or yellowish coating which covers it, and especially by its characteristic edges. These are detached to a varying depth, but always enough at some spot to enable the point of a probe or edge of a spatula to be passed under them; they are thin, and marked by a fine yellow border, similar to fresh butter. Moreover the base, even if infiltrated, is not indurated like that of the syphilitic chancre.

Simple chancre is rarely single ; the lesions, becoming easily inoculated, multiply and become much greater in number than in the case of syphilitic chancre.

The condition of the lymphatic glands varies ; sometimes they are painless and hardly perceptible, having retained their normal consistency ; at others they are often painful on movement and pressure, voluminous and suppurating (chancrous buboes).

The secretory products of multiple chancre contain a more or less abundant quantity of Ducrey's bacillus. The elements of this bacillus, measuring 1μ 5 in length by 0μ 5 in width, are isolated or united in fine chains of 2 or 3, with rounded extremities, resembling the figure 8 ; they are easily stained by Nicolle's method (gentian violet and tannin). Their demonstration is not easy, and can only be done satisfactorily by an expert bacteriologist.

A very important characteristic of simple chancre is the possibility of indefinite inoculation on the bearer, as long as the healing process is not advanced. Inoculation is made by means of a lancet or vaccination needle, intra-epidermically, or by superficial and slight scarification. Care must be taken to avoid both accidental contamination of the inoculated spot and reinoculations of the experimental chancre, by covering the inoculated region with a watch-glass held in position by a strip of diachylon plaster. At the end of the first day a red inflammatory areola appears at the inoculated point, having nothing characteristic about it ; but on the third day, in the centre of the areola, the epidermis is raised in a small pustule filled with turbid fluid ; on the fourth day, the fluid has become clearly purulent ; the small pustule bursts and leaves a cup-shaped depression, with well-defined borders ; during the following days, the chancre increases in size and depth, its borders become detached, and there is basal suppuration. Naturally, directly the experimental lesion has acquired sufficiently clear characteristics—

that is to say, on the third day, or at latest on the fourth or fifth—its progress should be arrested, which can easily be done by cauterising it fairly deeply with the thermo-cautery.

Another characteristic of simple chancre is its short incubation period. I have already stated that a syphilitic chancre is the result of intercourse fifteen to twenty days previously at a minimum, whereas simple chancre appears two or three days after coitus. Therefore, if it can be proved that no sexual relations have taken place within the five or six days preceding the development of ulceration of the genital organs, this cannot be a simple chancre.

In fact, there are rarely many difficulties in diagnosing simple chancre ; but the proof of its presence does not mean that the patient has escaped syphilis. Indeed, as Rollet has shown, the difference in the duration of the incubation periods of simple and syphilitic chancres produces consequences of considerable importance from the theoretical, as well as from the practical, point of view, which are as follows : the two viruses having been inoculated simultaneously during the course of a single coitus, may give rise to mixed infection ; the simple chancre appears first at its normal time, and develops in the usual way, but at the end of the syphilitic incubation period, the syphilitic chancre develops in its turn, blends its characters with those of the simple chancre, and gives rise to general syphilitic infection.

In such a case, the simple chancre does not at first differ in any way from that which results from inoculation of its own virus. Very naturally, therefore, the medical man diagnoses simple chancre ; then, at the end of fifteen to twenty days, the ulcerative characteristics become modified, the base becomes hard, without any error of treatment or secondary infection the surface dries up, and its borders are less detached sometimes being completely levelled.

A *mixed chancre*, according to the happy expression of Rollet, is thus formed; the lymphatic glands, which have been immune up to then, become hard, but not painful.

It is not always easy to observe the transformation; this can only be done by careful and repeated examinations; sometimes, at the end of several days, there is no further doubt; at other times, the diagnosis remains uncertain. As these chancres are generally much infected, it is difficult to search for the spirochæte.

As long as any doubt persists, anti-syphilitic treatment should be postponed, and sometimes it is only the appearance of roseola and secondary symptoms which enable the diagnosis to be settled.

Ecthyma of the genital organs is rare, but not absolutely exceptional. It generally affects the penis, most frequently in the form of scabs. The scab, thick, greyish, often adherent, covers a regularly rounded ulceration, with well-defined edges, occasionally detached. The most noticeable characteristic is the existence of abundant suppuration under the crust, forming a more or less adherent layer over the whole surface of the ulcer; below this, the base of the ulcer is bright red, bleeding easily, and a little uneven. It is not indurated. Ecthyma of the genital organs is often accompanied by swelling of the inguinal glands, which are painful on pressure. It coincides most frequently with ecthymatous lesions of other regions, especially of the legs, the existence of which may aid diagnosis.

Scabies, which has a predilection for the human genital organs, generally causes small papules covered with greyish scabs. These lesions cannot be confounded with chancre, as they are generally elongated, raised, and non-ulcerous. When, exceptionally, they develop into large pustules, these and the ulcerations which succeed them have all the characteristics of ecthyma.

The existence of indubitable signs of scabies does not imply that all co-existent ulcerations of the genital organs are of the same origin. There is risk of syphilitic inoculation with scabies, on account of the solution of continuity it causes, and, in patients suffering from itch, syphilitic chancres are often multiple, owing to the multiplicity of these solutions of continuity.

Common Excoriations of the Genital Organs, infected as the result of uncleanliness, may become surrounded by an inflammatory infiltration simulating chancrous induration ; careful examination, however, will show that there is no true induration. Wet dressings applied for two or three days, and the suppression of all causes of irritation, will induce all trace of inflammation to disappear, and show that it is merely a simple lesion, without genuine induration.

Gangrene of the Genital Organs begins with apparently simple ulcerous lesions, often with basal infiltration, but is soon revealed by the presence of a greyish or blackish plaque, surrounded by an infiltrated zone which is liable to spread. At the same time, there are usually general symptoms and often high fever. There is no possibility of confusion with syphilitic chancre. There are cases, however, in which the gangrene situated on the gland is accompanied by intense œdematous inflammation of the prepuce as in concealed chancres of the prepuce. The existence of the eschar is only manifested by a discharge of sero-purulent or sanious fluid from the preputial orifice, resembling the secretion of an ulcerous balanitis. If this fluid is collected, its gangrenous odour attracts attention and aids in determining the presence of a sub-preputial eschar.

Gangrenous lesions of the genital organs may develop with syphilitic chancre ; hence the diagnosis of gangrene does not exclude that of chancre. As chancre, when complicated by gangrene, loses all its objective characteristics, and further, as the presence

of various micro-organisms, and specially of spirilla, on the surface, prevents the discovery of any treponema which might exist there, there may be doubt as to the presence of a chancre. In a case of gangrene of the genital organs, when prolonged observation did not enable me to detect any secondary syphilitic manifestation, the Wassermann Reaction, made on several occasions, was positive once, partially positive another time, and finally became and remained negative. I was told of another altogether similar case by Dr. Ristitch. There is, thus, reason to suppose that gangrene of the genital organs may cause a temporary Wassermann Reaction, and, until the most complete study has been made of the case, the diagnosis of syphilis should be suspended till the secondary manifestations have appeared to corroborate it.

Ulcerations induced with the Object of Simulation may present objective characteristics resembling those of syphilitic chancre. All the same, it is rare for the resemblance to be close. In the few cases I have observed it was generally a question of burns from a lighted cigarette, a traumatism which produces regular rounded ulceration resembling simple, more than syphilitic, chancre. Even when, as the result of repeated irritations, the simulator succeeds in inducing a certain degree of infiltration of the ulcerative base, this is more diffuse than that of syphilitic chancre, and the absence of treponema is against this diagnosis.

As a rule, the imitation is rougher and more clumsy still. I recently saw a dry, adherent, and circular eschar on a soldier, who stated that it was due to sexual intercourse some days before, and hoped that, thanks to this lesion, he would be passed as syphilitic and sent to hospital for some time. Even the character of the eschar, which was adherent and impossible to detach, as well as its almost circular configuration with an angular prolongation at one

peripheral point, testified to its artificial origin. I could not get an acknowledgment of trickery, nor a demonstration of the caustic employed, but I have reason to believe that it was produced by oxalic acid.

Erosive and Ulcerous Balanitis is manifested by sero-purulent secretion and erosions: these erosions are multiple, irregular, often confluent, without basal induration, and can hardly be confused with syphilitic chancre. Their acute course, rapid cure by simple means, and the absence of enlargement of the inguinal glands, are points which settle the diagnosis.

Epithelioma is rare on the genital organs. It may be observed there, however, even in men called up for military service.

It commences either as a smooth, projecting tumefaction, or as a wart-like growth, which evolves slowly. It is only at the end of several months that ulceration appears: this is of variable extent, is often covered by a sanious secretion, has an irregular base of wood-like hardness. The prolonged duration of the affection, and, in default of a precise history from the patient or confidence in his assertions, the characteristics of the basal ulceration and extreme hardness of the edges should remove any suspicion of syphilitic chancre from the diagnosis.

Syphilitic lesions may sometimes be confused with infective chancre.

Erosive **Mucous Plaques** of the glans and prepuce consist, like the chancre, of superficial and circular loss of substance; but they are even more superficial than the chancre, while their border, on the contrary, is often more defined, the limit between the healthy tegument and erosion, even if the plaque is not depressed, is abrupt, and marked by a more or less definite raised border. By means of careful palpation, it can be shown that their base is of firmer consistency than the adjacent parts, but it is nothing like that of chancrous induration. Sometimes, however, in the

midst of the erosive plaques with hardly any infiltration, one will be encountered which is generally larger, with a slightly raised border and a firm base ; this is a mucous plaque developed on the site of the chancre, and by its direct transformation before complete cicatrisation.

Certain **tertiary ulcerations** of the prepuce and especially of the glans simulate chancres so much that they have been regarded as recurrences. Alfred Fournier has called attention to them under the name of *chancriform syphilides*, and has made use of their existence as an argument in support of his too absolute opinion, that a chancre never recurs.

Appearing always several years after the initial chancre, sometimes on the site of the cicatrix, these syphilides generally begin as a rounded projecting tumefaction, which softens and ulcerates at the centre. In a few days, the ulceration attains the average size of a small hazel-nut ; its form is rounded, its surface depressed, sometimes deeply excavated, often irregular and mammillated, its borders project, clearly marked, not detached ; it rests upon a firm infiltrated base ; the infiltration projects beyond the ulceration and forms a rounded nodule below it, differing from the induration of a chancre.

On the whole, the ulcerative characteristics are those of a gumma rather than a chancre, and the histological structure, in two cases I was able to study, was that of gumma.

The absence of treponemas in the scrapings from the ulceration, the positive Wassermann Reaction from the beginning of the lesion, the tendency to persistence until treatment is begun, and the rapid cicatrisation under its influence, indeed all the biological and evolutive characteristics, as well as the details of the clinical aspect, are those of ulcero-gummatous tertiary lesions.

A certain number of the male bearers of these

ulcerous lesions blame a suspicious coitus as the cause of their appearance. Finger and Landsteiner inoculated tertiary syphilitics with the products of recent syphilitic lesions and produced at the point of inoculation, not a chancre, but a tertiary lesion, thus seeming to give some probability to the assertions of these patients. This is a question requiring investigation, which we need not consider further at present. It is none the less true that these lesions differ profoundly from chancre, and that, contrary to genuine chancrous recurrences, they do not give origin to a fresh attack of syphilis with secondary symptoms.

The Pseudo-chancre of Syphilitics treated by Arsenobenzol.—It is not unusual to see an ulcerous lesion appear in syphilitics, who have been subjected to arsenical injections, at the same point at which the initial chancre was situated and somewhat resembling the syphilitic chancre. Some too zealous partisans of arsenical medication have, without hesitation, regarded it as a second chancre, and a proof of the sterilisation of syphilis by arsenobenzol.

The following is what occurs with this lesion, according to facts I have observed.

Some variable time after the initial chancre and the arsenical treatment, often some days after intercourse with a syphilitic or non-syphilitic woman, an ulceration appears at the site of the chancre, which in a few days spreads and attains the dimension of a sixpence, a shilling, or more ; sometimes in the neighbourhood of the first, one, or more rarely two, other ulcerations appear within the space of a few days.

When it has come to a head, the round or slightly oval, but always regular and clearly defined ulceration presents a regular or slightly mammillated base, covered with exudation or a whitish-grey detritus, rather creamy, and fairly easy to detach. When this exudation is removed the base appears red and sometimes bleeds easily. The borders are often slightly

raised, clearly cut out, and sometimes slightly detached in places.

The lymphatic glands are of normal size or slightly enlarged, unless they have remained enlarged after the healing of the initial chancre.

The ulceration tends to persist for several days, rarely for some weeks; it heals sometimes under moist dressings of boiled water, but at others only responds to mercurial treatment.

Research for the treponema in the ulceration scrapings gives uncertain results, even after cleansing the surface.

The Wassermann Reaction may be either positive or negative.

If the patient is left without treatment, there is no evidence of secondary symptoms during the following weeks, as there would be if it were a case of syphilitic reinfection.

Such is the ulceration which has been erroneously regarded as a recurrent syphilitic chancre: it differs from a chancre in all its objective characteristics, by its appearance a very few days after coitus, the usual absence of treponemas, and, finally, by the absence of secondary symptoms at the end of the classical period of secondary incubation.

On the other hand, it was unknown before the use of arsenobenzol, and is only observed in syphilitics treated by the arsenical method. It cannot be attributed either to insufficient or excessive doses of arsenobenzol, for I have seen it appear in patients who had only received two injections of arsenobenzol, representing about 1 gr. of this substance, and in others who had received 7, 8, or even 12 injections of 2, 4, or 5 grammes.

This lesion requires further study. At present, it may be considered as one of the consequences of arsenical treatment, a consequence without any great clinical importance or apparent gravity, and of which

the pathogenesis and conditions of development are not yet completely determined. But it should not be considered as a morphological deviation of chancre, nor as a recurrence of syphilitic infection. Its existence, without denying the possibility of a syphilitic reinfection after treatment by arsenobenzol, should make one very cautious in interpreting cases of second chancre, and permits one to challenge a certain number of the observations published in support of the occurrence of this reinfection.

EXTRA-GENITAL CHANCRES

The syphilitic chancre may occupy all regions of the body without exception. The frequency of extra-genital chancres, their aspect even, which is unusual or at least deceptive in many of them, and especially the anomalous manner of contamination they generally show, give a special interest to their study.

Extra-genital chancres do not appear to be very frequent in the Army, according to Carle's statistics.

Nevertheless, despite their infrequency, owing to the difficulties of diagnosis they sometimes present, it is necessary to give an adequate account of their two most usual localisations, these being the only places in which, up to the present, I have observed them in soldiers.*

The first, chancre of the lips, is important, because of its frequency ; the other, chancre of the tonsils, on account of the diagnostic errors to which it is liable.

Chancre of the lips is not necessarily non-venereal

* Mention must, however, be made of chancre of the beard (cheek and especially chin), usually the result of inoculation by the barber, by means of a razor or shaving-brush which has been used to shave a syphilitic. This chancre is often extensive and covered with scabs, below which is found a vegetating or oozing surface; its base is sometimes red, of inflammatory aspect, but manifestly indurated. The most important diagnostic characteristic is the adenopathy (sub-maxillary or sub-mental, according to the position), often enormous, which accompanies it.

any more than chancre of the tonsils ; both may be, and often are, transmitted by kisses or the projection into the mouth of saliva charged with syphilitic products.

Still, the mere fact of the localisation is sufficient index for admitting the possibility of contamination by accidental non-venereal contact (tumbler, fork, pipe, end of cigarette, dentist's instrument, etc.) ; an inquiry is the only way of determining whether this presumption is well founded. This inquiry, however, is often extremely difficult, especially with subjects whose interest it is to disguise the real cause of contamination and attribute their malady to "innocent" contact.

Chancre of the Lips.—A syphilitic chancre may occupy both lips, but is much more frequent on the lower than on the upper lip ; its most usual position is in the centre involving both cutaneous and mucous portions.

Of round shape, it projects from the free border of the lip in the shape of a pastille, the fore part of which is covered by a brownish, adherent scab ; removal of the scab is painful and sometimes causes bleeding. The surface is generally bright red, firm, smooth, regular, and clearly defined.

If the patient's mouth is opened, the posterior part of the ulceration, which continues the contour of the anterior part and completes the circumference, appears moist and red, or covered by a whitish-grey coating, often resembling that of mucous plaques.

The ulceration, of variable extent, from the size of a lentil to that of a sixpence or larger, rests on a tumefied base ; the lip is deformed by this tumefaction and everted.

On palpation, the base of the chancre is hard. The induration must be looked for in the same way as that of chancre of the genital organ and is easy to perceive, but often surrounded by an infiltrated zone, which

must be pressed upon in order to distinguish the induration itself.

The *adenopathy* of chancre of the lips is always considerable and can be observed from a distance. It affects the sub-maxillary or sub-mental glands, forming a rounded eminence, often the size of a pigeon's egg. Palpation enables one to recognise one or more of the glands surrounded by an inflammatory zone of periadenitis, which sometimes seem to be adherent to the maxillary bone.

The *diagnosis* of chancres of the lips is easy. Its development within a few days, often following an excoriation which has been present for some time, and which has rapidly become "festered," the eversion of the lip, basal induration, and considerable enlargement of the glands, prevent all confusion with cancerous or other ulcerations of the region. Simple lesions, inflamed by local irritation and especially by unsuitable dressings, may deceive, but their form is rarely as regular as that of chancre, and they are accompanied neither by marked basal induration nor by voluminous adenopathies.

Microscopic examination of the scrapings is of little value in these cases, for the lips harbour a large number of different parasites, especially spirilla, which dissimulate the presence of the treponema or may be confused with it.

Chancre of the Tonsil.—Tonsillar chancre is rare, but is liable to such frequent diagnostic errors that the syphilis to which it gives origin is generally not recognised until the secondary symptoms appear.

It occupies one tonsil only, covering it almost entirely, but rarely extends beyond it. Its usual size is that of a sixpenny piece ; its shape is round, oval, or irregular. It sometimes appears as an erosion of a greyish, opaline, or red coloration, regular and smooth at the base, or made uneven by the irregularities of the tonsillar surface ; at other times it may be

ulcerous, even deeply so, of a reddish-brown or grey coloration ; occasionally it is covered by a pseudo-membranous exudation, white, thick, adherent, resembling that of diphtheria.

Whatever its clinical form, tonsillar chancre always has two important characteristics :

(1) Basal induration, appreciable with the finger (covered for precautionary measures with a rubber finger-stall), or with a rigid instrument, tongue-depressor, etc., which should be handled gently and not pressed on its circumference, as in the examination of chancre of the genital organs, but on the surface itself.

(2) Enlargement and induration of the lymphatic glands in the region of the angle of the jaw are often appreciable to sight and always to palpation.

Contrary to most other localisations of syphilitic chancre, tonsillar chancre is frequently painful, owing both to its seat upon a mobile region and to the secondary infection of its surface. While often slight at the onset, within a few days the pain becomes acute, and persists for several weeks.

The *diagnosis* of chancre of the tonsil depends more on the basal induration and sub-maxillary adenopathy than on the characters of the ulceration, which vary in different cases and may simulate the most diverse affections : simple tonsillitis, Vincent's angina, diphtheria, tonsillar abscess, tertiary syphilides, tuberculous ulcerations, even epithelioma of the tonsil and gangrene of the pharynx.

It is impossible here to enter into the differential diagnosis of these different affections, a diagnosis which is often difficult, even for skilled specialists, syphilologists, or laryngologists. I consider that, whenever a medical man has the slightest suspicion of chancre of the tonsil, he should, without delay, send the patient for examination by a syphilologist or laryngologist. I cannot emphasise too much the difficulties encountered in the bacteriological examination of such

lesions : it is practically impossible to discover the treponema in the scrapings of tonsillar chancre ; on the other hand, numerous spirilla may resemble it and deceive an observer who is not sufficiently wary ; finally the existence in the scrapings of clearly differentiated micro-organisms, even Loeffler's bacillus, is not sufficient to eliminate the possibility of a chancre evolving at the same time as another tonsillar infection.

SECONDARY SYPHILIS

Syphilitic chancre, with its satellite adenopathy, constitutes the whole symptomatology of primary syphilis ; it may even be already cicatrised before any clinical sign reveals general infection of the economy.

But after a period, called that of *second incubation*, which from the beginning of the chancre is generally forty-two to forty-five days, roughly six weeks, general syphilitic symptoms begin to appear in cases which have not been modified by intensive treatment, constituting the *secondary period* of the disease.

In this chapter I shall limit myself to summarising the principal manifestations of secondary syphilis. For the military surgeon, they are relatively less important than the chancre, not because they are less frequent in the Army, but because diagnosis is generally easier, owing to the history of the initial chancre, generally easy to obtain, because their clinical forms are less varied than those of chancre, and also, because the Wassermann Reaction is almostconstantly positive.

General Phenomena

The secondary period is accompanied by general phenomena : fever of variable type, which, in rare cases, may simulate typhoid, more or less marked general malaise, anæmia, the hæmatological characters of which

are still indefinite, emaciation, often headache varying in intensity, generally nocturnal, sometimes continuing during the night and preventing sleep; the lymphatic glands become enlarged and can be felt in all regions accessible to palpation, especially at the nape of the neck, in the neck, and above the olecranon. The viscera are subjected more or less to the action of the pathogenic agent of syphilis; they react sometimes in the form of clinically appreciable disturbances; as a rule, however, no symptoms reveal their implication.

Cutaneous Lesions

The secondary period is especially that of cutaneous lesions.

These lesions (*secondary syphilides*) have the following general characteristics: rounded form; a tendency to form circles or semicircles when grouped on neighbouring points; red coloration, due to the combination of cutaneous congestion with a certain degree of dermic infiltration and pigmentation, a coloration which has been compared to that of copper, or lean ham; sometimes, but less often than is generally believed, there is, at the periphery, a slight epidermic elevation (Biett's collar); the tendency to generalisation or at least to very considerable extension, contrasts with the regional limitation of tertiary lesions; the tendency of the lesions to polymorphism, is very great in certain papular forms; the absence of pruritus; finally, the tendency—an exception being made to a particular form of syphilides occurring in malignant syphilis—to heal without cicatrisation, but often leaving a cutaneous pigmentation which persists for some time.

The co-existence of a positive Wassermann Reaction may aid diagnosis.

The cutaneous lesions of secondary syphilis present the most varied dermatological types.

Roseola.—The erythematous type, or roseola, is

the most simple and the most frequent of all secondary syphilides. Generally appearing towards the forty-fifth day after the beginning of the chancre, syphilitic roseola first appears on the abdomen, then the internal surface of the thighs and trunk, afterwards extending to the neck and upper arms. The first pale, round elements may be difficult to recognise, and should be looked for carefully; they soon multiply from day to day, till in a few days the eruption is complete. The medical man, who has been obliged to await the appearance of roseola before determining the diagnosis of an ulceration of the genital organs, should look out for it about the fortieth day after the commencement of the chancre; when he has detected a few red spots all doubt will be removed by their rapid multiplication.

Roseola consists of round spots, sometimes with ill-defined borders, the size of a lentil to that of a threepenny piece, isolated from each other; these spots are sometimes flat (*macular roseola*), sometimes raised (*papular roseola*), or sprinkled with small projections (*granular roseola*), sometimes raised and of a paler colour (Alfred Fournier's *urticarial roseola*).

The colour of roseola disappears under pressure, leaving a slight yellowish macule.

If not treated, syphilitic roseola persists for several weeks; whereas, under the influence of treatment, it quickly fades and disappears gradually, without causing desquamation or leaving any trace beyond a very minute macule, faintly pigmented, which disappears in its turn in a few days.

Along with this form of generalised roseola with round elements of small dimensions, which appears towards the seventh week of syphilis and is never reproduced during the whole course of the disease, another erythematous syphilide must be mentioned, known under the name of *recurrent* or *delayed roseola*. This appears at varying times, from three months

to fifteen months, rarely later, and may recur once or twice; it consists of rose-coloured spots, paler than those of early roseola, and of larger dimensions, reaching the size of a two-shilling piece. These spots, like those of early roseola are sometimes nummular and of uniform coloration over their whole surface; they are often circinate, their rose contour forming a more or less complete crown around a zone of normal skin. The spots disappear on pressure; they are much less numerous than those of early roseola, and are often limited to one region of the body, principally the abdomen, but sometimes to the limbs.

This recurrent roseola may develop in patients who had previously presented early roseola at the normal date; but it is observed much more frequently in subjects who have been given arsenobenzol at the beginning of syphilis, and, not having followed regular treatment, have never had roseola. The interval between treatment and the commencement of delayed roseola is most variable, being three to four months most frequently. It appears that arsenobenzol, in inhibiting the appearance of the symptoms, has merely retarded the eruption, which, at the period at which it eventually appears, no longer does so under the form of generalised early roseola.

Diagnosis of Syphilitic Roseola.—Roseola, whether early or delayed, can hardly be confounded with any of the great exanthems, *morbilli*, *rubella*, which are easy to recognise by their exanthematous characteristics, rapid appearance, and general concomitant phenomena.

Medicamental Erythemas, induced by various drugs (quinine, antipyrine, chloral, etc.), may appear in the form of isolated spots, resembling roseola; their rapid development and especially the sensations of heat and pruritus which accompany them, distinguish them from this form of syphilide.

Gibert's Pityriasis rosea is frequently mistaken for a

syphilitic roseola. It is only necessary to bear in mind the existence of this affection and the possibility of confusion in order to avoid it. Pityriasis rosea is characterised by a more or less abundant eruption of rose spots, of very varied dimensions, round when small, more frequently irregularly oval as soon as they attain the size of a sixpence, with rose-coloured contour, and bright chamois yellowish centre. The epidermis, which is always intact in syphilitic roseola, is slightly creased in pityriasis rosea, and, when the skin is stretched in the direction of the long axis of the plaque, it takes on the appearance of crepon ; moreover, without actually desquamating, it is often raised at the periphery of the chamois-coloured zone forming a fine white border. Pityriasis rosea generally commences with a large oval patch (Blocq's "mother plaque"), which may attain the size of a two- to five-shilling piece ; this may appear on any part, usually the upper portion of the thorax, from whence other spots extend progressively to the abdomen. The former existence of syphilitic chancre and the co-existence of mucous plaques are not sufficient to exclude the presence of pityriasis rosea, for this disease sometimes develops during the course of secondary syphilis, without any accountable reason.

Papular Syphilides.—The cutaneous papular lesions of secondary syphilis are frequent and of varied aspect.

Several very different kinds must be described :

1. The *syphilitic plaques* of Bazin and Legendre, characterised by circular prominences, with sharp contours, round or oval, and red or brownish periphery ; the slightly depressed centre, generally of a brown colour, often shows superficial desquamation. These lesions appear at a variable date of the secondary period, sometimes before the roseola, but more frequently during its course and decline, and are often situated on the neck and upper part of the trunk.

Lesions of the palms of the hands, frequent during

the secondary period, generally under the defective name of *palmar psoriasis*, must be included amongst syphilitic plaques. They consist of a central zone stripped of its epidermic covering and surrounded by a circular squamous elevation of variable thickness. They are situated symmetrically on both hands in varying numbers, sometimes being very numerous. They may appear at any time in the secondary period, and are cured completely by syphilitic treatment.

In the folds (axillæ, umbilicus, inguino-crural region, inter-gluteal fold, commissures of toes), the plaques become exudative or ulcerated, and their appearance is absolutely identical with that of plaques of the external genital organs; like them, they may become hypertrophic.

In the beard and scalp, they are covered by raised scabs, sometimes forming thick and oozing patches of varying size.

Syphilitic plaques are frequent on the genital organs, and sometimes remarkably recurrent. Of erosive form on the prepuce and glans, where they resemble mucous lesions (hence the name of mucous plaques), on the scrotum they are erosive or ulcerous, often hypertrophic, prominent, and of papillomatous appearance.

2. *Papular syphilides with large papules*, which often begin before the disappearance of the roseola, are characterised by flat papules, rarely very prominent; their dimensions may reach and exceed those of a large pea or a small hazel-nut; generally well defined, surrounded by a collar of epidermic desquamation, they are of a more or less deep reddish-brown colour and of firm consistency. After a duration which is only limited by treatment, they subside and their colour fades, but a brown pigmented patch remains for several weeks, or months; sometimes wheals, when the eruption is situated on the trunk.

Scales of varying thickness may develop on the

papules, resembling sometimes those of pityriasis, sometimes these of psoriasis ; the syphilides then take the name of *papulo-squamous syphilides.*

The large papular syphilides may be situated on any region of the body, but have a certain predilection for the body, and, in alcoholics, for the face.

They are indicative of grave syphilis, and nearly always coincide with an abundant lymphocytosis of the cerebro-spinal fluid (Ravaut).

3. *Syphilides with small papules* always appear after roseola, sometimes at the moment of its disappearance and on the spots of the roseola. They have a tendency to form irregular groups, reminding one of constellations of stars, the groups being irregularly distributed over the trunk, but rarely on the limbs.

Their elements, developed around the hair-follicles (hence the name of *follicular syphilides*) vary in appearance in different cases, often indeed in different groups of elements in the same patient, even in different elements of the same group ; thus exhibiting a polymorphism more pronounced than in any other syphilide.

Some are prominent, acuminated, or smooth, covered by adherent epidermis, sometimes shining (*lichenoid syphilides*, still erroneously called syphilitic lichen) ; others have a slight central desquamation corresponding to the orifice of the hair-follicle, or a very small pustule, which dries up and is replaced by a thin scab (*acneiform syphilide*), also wrongly called syphilitic acne).

These elements do not exceed a grain of millet-seed in size, hence the name *miliary syphilides* which has been given them.

Small papular syphilides are often very resistant to treatment, even to an intensive course of arseno-benzol.

They may be confused with Wilson's lichen, from which they differ essentially, besides their objective

characteristics, in the absence of pruritus, and especially with follicular tuberculide or lichen scrofulosorum, of which the elements occupy the same positions, and are disposed in the same way, but are larger and tend to suppurate; moreover, lichen scrofulosorum is only found in patients with active tubercular lesions, specially adenitis and suppurative osteo-arthritis.

Vesicular, Bullous, and Pustular Syphilides.—These are rare; the diagnosis rests upon the co-existence of syphilitic lesions in other situations, and on the previous existence of chancre.

Ulcerative Syphilides.—Ulcerative lesions are rare during the secondary period. They constitute a special form of syphilis, known under the name of *malignant syphilis*, which some authors have wrongly wished to separate from syphilis.

They commence with flat nodules of a red or brownish colour which rapidly soften, forming round ulcers with sharply cut borders and an irregular base, covered by pus or by dry grey scabs, often limpet-shaped; at the circumference of the ulcer is a red zone of infiltration of variable extent. These ulcers may reach three to four centimetres in diameter or more. They leave behind them deep circular cicatrices, often surrounded by a pigmented zone.

The ulcers may be irregularly distributed all over the body; they have, however, a predilection for the lower limbs. On the face, where they are seen but rarely, they sometimes cause extensive destruction and leave considerable deformity behind them.

Malignant syphilis occurs in patients debilitated by privations, serious illnesses, and in "lymphatic" subjects. It appears to be but rarely observed in the Army.

Pigmentary Syphilide.—The pigmentary syphilide is much more common in a woman than a man, but it frequently attains a size and intensity in the latter which is altogether exceptional in a woman.

Contrary to the teaching of Alfred Fournier, who regarded it as a lesion *sui generis*, it is to-day well established that the pigmentary syphilide always follows *in situ* a previous cutaneous lesion, most frequently roseola, more rarely syphilitic plaques of the skin or papular syphilides. It is characterised by a greyish-brown coloration, of varying intensity, occupying the neck symmetrically; on this pigmented and patchy surface are disseminated round areas, the colour of which, by contrast with the surrounding pigmentation, seems paler than that of the normal skin; these areas, of a round or oval form, are of variable dimensions, generally on an average that of a large pea; their boundaries are well defined; their site and dimensions correspond exactly to that of the eruptive element, which preceded the pigmentary syphilide.

In another variety of the pigmentary syphilide the pigmentation forms a border to the less dark zones.

The favourite site of the pigmentary syphilide is the neck, principally on the anterior and lateral surfaces; from there it may extend to the upper part of the thorax and on to the back.

In very extensive forms, which are relatively frequent in man, it is not limited to the cervical region, but occupies the periaxillary regions in front and behind, sometimes the groins, and may even extend to the trunk.

The pigmentary syphilide, once established, persists for several months, and only disappears very slowly, no matter how intense the antisyphilitic treatment. It is of great value in diagnosis.

The co-existence of cerebro-spinal lymphocytosis, established by Ravaut, gives a certain prognostic importance to the pigmentary syphilide, and is an indication for energetic treatment, in order to prevent the later development of serious lesions of the nervous centres.

Syphilitic Alopecia

Alopecia is frequently a symptom of secondary syphilis, especially in cases not treated at all, or imperfectly treated.

It appears without any apparent previous lesion of the scalp, without desquamation, as well as without objective phenomena, such as pain or pruritus ; the fall of hair, which becomes more and more abundant, leads to the production of areas of alopecia scattered irregularly over the scalp, resembling the empty spaces in a badly planted wood.

It may be observed exceptionally in the beard. It frequently coincides with a pigmentary syphilide of the neck.

This form of alopecia is almost pathognomonic of syphilis, for it is altogether exceptional in other general conditions (tuberculosis, convalescences from severe illnesses, etc.) which cause diffuse loss of hair. The bald areas of alopecia areata are larger and smoother than those of syphilis.

It may, therefore, aid in the diagnosis of syphilis, and is worthy of attention as it may be the first syphilitic manifestation noticed by the patient. Indeed, it is not rare to see it appear in subjects who have had a dwarf chancre which healed in a few days and was not noticed, who, probably, have not had any cutaneous syphilide, and in whom the most careful examination has only revealed a few slightly enlarged lymphatic glands and one or two small syphilitic plaques of the mouth.

The presence of this alopecia is an indication for the most careful search for all the signs of syphilis, even the slightest, and, in the absence of any other sign, examination by the Wassermann Reaction.

Syphilitic alopecia generally begins during the third month of syphilis ; it always heals without leaving any trace behind. It may heal spontaneously,

but cure is hastened by mercurial, and especially by arsenical treatment, which is sometimes followed by a regrowth of hair more abundant than before the syphilis.

Lesions of the Nails

The nails may be attacked during the course of secondary syphilis, become cracked, detached, or hypertrophied. More frequently, after periungual syphilides, swelling of the bed of the nail (perionyxis) may develop.

Lesions of the Mucous Membranes

All lesions developed during the course of secondary syphilis on the visible mucous membranes may be reduced to two; diffuse erythematous inflammations, often transient, seen usually on the pharynx, and the *mucous plaque*.

Wherever situated, the mucous plaque begins as a round lesion with slightly raised edges and an eroded, slightly depressed centre. The erosion, of variable extent, is red and exudative. The border is red on mucous membranes that are simply moist; on those of the digestive tracts, its constant impregnation by saliva gives it whitish or opaline colour.

The configuration of the parts which are the seat of mucous plaques modifies their form, and makes them irregular or fissured, especially on the lips.

Local irritations and infections may modify their appearance and cause deep ulceration, or on the other hand, hypertrophy and a papillomatous appearance (hypertrophic mucous plaque, condyloma latum).

Lesions of the Buccal Mucous Membrane.—Mucous plaques may occupy different regions of the buccal cavity. On the *lips* they are situated either on the commissures, in the form of round erosions with a raised border; they are rarely hypertrophic, except in patients who smoke much and place the cigarette

or pipe at the corner of the mouth : or on the free border, in the form of round erosions, with a white margin, a deep red and flat base, exudative and sometimes covered with a scab ; this last localisation occurs almost exclusively in smokers.

On the *internal surface of the cheeks* the plaques are usually erosive, round, or slightly irregular, red in the centre ; the border and a more or less extensive portion of the centre is often white, sometimes like silver, resembling leucoplakia.

Mucous plaques must not be confused with mercurial stomatitis, the lesions of which first affect the gums but may also occur on the cheeks ; with aphthae (thrush) which consist of round plaques, covered with a white creamy or slightly yellow deposit and evolving rapidly ; with lesions artificially induced (burns from a cigarette, acid, etc.), which are round, regular, and covered with a white deposit, sometimes detached at one part (rupture of the phlyctenule) and healing rapidly ; with the plaques of leucoplakia, which are more irregular, more extensive, and occupy principally, either the neighbourhood of the labial commissure, or that of the large molars. This last diagnosis is of real importance, a certain number of soldiers attacked by leucoplakia, due to former syphilis, exploit their lesions to gain admittance to hospital, when there is no reason for this, the lesion being non-contagious.

On the *tongue*, mucous plaques often assume a special aspect, owing to the papillary structure of the mucous membrane : they are round or oval, clearly defined, flat, with no trace of papillæ (*depapillated plaques*). Sometimes they are erosive, regular or irregular, surrounded by a white or *opaline* border.

Mucous plaques may be confused with marginate exfoliative glossitis. This differs in the irregularity and variability of its contour, which has been compared with that of a geographical map, and by its white, slightly raised, clearly marked border, the

eccentric and irregular progression of which extends from day to day; with leucoplakia, which has been referred to above; with Wilson's lichen, a much rarer and more persistent affection, the lingual lesions of which coincide with the white spots on the mucous membrane of the inner surface of the cheeks, and with very pruriginous cutaneous lesions.

Lesions of the Pharynx

These are of great frequency, more so perhaps than those of the mouth.

On the *soft palate*, they consist in mucous plaques of regular or irregular form, generally opaline, as if a slight coating of pale grey paint had been spread over the mucous membrane; they are rarely erosive. They often attain considerable dimensions, forming a large surface of vivid or deep red on one or both of the anterior pillars, limited by a semicircular, slightly projecting border, forming a kind of large arcade (*giant plaques* of the soft palate).

Sometimes, at the beginning of syphilis, a diffuse bright redness is observed.

The *tonsils* may be the seat of various lesions: they are very often *hypertrophied*, voluminous, irregular, of almost normal or reddish colour, and firm consistency, more pronounced than in common tonsillar hypertrophy. The mucous plaques, sometimes opaline, sometimes erosive, are often very numerous, sometimes small and difficult to discover.

In certain cases the lesions attain very considerable development: the plaques occupy almost the entire tonsil, and are covered by a thick, greyish white, adherent deposit, beneath which the tonsillar tissue is ulcerated and bleeds easily. This diphtheroid form of syphilitic angina may be confused with diphtheria, and with Vincent's angina.

The last confusion is the easier because Vincent's

spirillar infection may be grafted on syphilitic lesions of the tonsil, or coincide with secondary syphilis.

Visceral Affections

Secondary syphilis may attack all the viscera and tissues ; I shall only describe the most important of the deep localisations.

Nervous Affections of varying intensity and gravity are frequent during the course of secondary syphilis.

Headache is extremely frequent, practically constant in untreated syphilis : sometimes frontal, sometimes occipital, in some patients it is so severe as to prevent sleep ; it is characterised by its occurrence or exacerbation in the evening or at night. It is often, but not always, accompanied by hypertension and lymphocytosis of the cerebro-spinal fluid, even if the headache is not very violent ; it is sometimes, but not always, relieved by lumbar puncture. In certain cases it is due to endo-cranial periostoses, and is then both intense and persistent.

Grave cerebro-meningeal symptoms may be observed during the course of secondary syphilis.

These symptoms assume various clinical types.

Hemiplegia, either preceded or not by premonitory signs, such as difficulty in speech, cerebral fatigue, or headache, occasionally commences suddenly. It is established progressively within a few hours, soon becoming complete, and at the same time intellectual obnubilation ends in more or less complete coma. It may be followed by death in some hours ; more frequently the patient recovers, but is often left with paralysis and contractures.

When affecting the right side of the body, it is often accompanied by aphasia, which is generally curable.

Of all the nervous manifestations of syphilis, hemiplegia is the one most likely to appear at an early date. It may precede other secondary symptoms and

occur even in the first days of syphilitic evolution : in a case of Millard's, which terminated fatally, the chancre had only been in existence eleven days.

At the post mortem, special lesions of the arteries at the base of the brain are found, as well as meningeal changes.

Facial paralysis, of peripheral type, is more frequent than hemiplegia ; it generally occurs in the second or third month.

Paralysis of the oculo-motor muscles is more rare, but may accompany facial paralysis.

These paralyses are the result of basal meningitis, causing compression of the corresponding nerves, as it produces compression of the optic and auditory nerves.

The spinal meninges participate in the process of basal meningitis.

Along with rare cases, manifested by definite symptoms of spinal meningitis and *acute meningo-myelitis*, there are other more common cases, in which the meningeal changes are not revealed by appreciable objective symptoms ; in these cases lumbar puncture shows the presence of *lymphocytosis of the cerebro-spinal fluid* and albumen in this fluid. Ravaut has shown the frequency of cerebro-spinal lymphocytosis in secondary syphilis and proved that it may indicate the later development of serious cerebro-spinal lesions.

The **sensory organs** may be attacked during secondary syphilis.

Deafness, tinnitus, and vertigo may be caused by lesions of the auditory nerve and labyrinth. These affections, to which attention has been directed since the use of arsenical preparations, were known of before the discovery of arsenobenzol, but appear to be particularly frequent in patients treated with this substance.

Optical lesions are much more common.

Iritis is the easiest to recognise, and the most apparent of all ocular lesions ; it generally develops between the

fifth to the tenth month after the chancre, usually about the sixth month, sometimes earlier, and must be regarded as indicative of particularly severe syphilis.

Generally unilateral, it is manifested by periorbital pains of varying intensity, often slight, by photophobia and more or less pronounced diminution of visual acuteness as well as by objective symptoms which any medical man, even if not versed in practical ophthalmology, must know and cannot fail to recognise : more or less marked pericorneal injection, change in the colour of the iris, which loses its brilliant appearance and takes on a greyish tint, contraction and immobility of the pupil, due to congestion of the iris or adhesions. Atropine dropped into the eye induces dilatation of the pupil ; but if adhesions are present, the dilatation is unequal and the pupil irregular.

Syphilitic iritis assumes various clinical forms (serous iritis, gummous iritis, etc.) into the details of which I cannot enter here. It is sufficient for me to point out the signs by which it can be recognised, for its gravity is such that every syphilitic patient suffering from iritis should be subjected to examination by an ophthalmic surgeon.

Again, iritis frequently accompanies lesions of the deeper portions of the eye, such as cyclitis and choroiditis.

Optic neuritis and *retinitis* are frequent during the secondary period of syphilis, even at the beginning. They are often unrevealed by any functional symptom, and can only be recognised by examination of the fundus of the eye. In default of the systematic examination of all syphilitics by an ophthalmologist, a large number of these complications pass unnoticed. I may add that they are accompanied by lymphocytosis of the cerebro-spinal fluid.

Secondary Syphilitic Icterus is characterised by its appearance in conjunction with generalised eruptions ; it is accompanied by phenomena of biliary retention, but

the gastric troubles of catarrhal icterus are generally absent. It usually terminates in recovery without any complication, within fifteen to twenty days; a few rare cases of grave icterus in secondary syphilis have been reported, presenting the ordinary symptomatology of this syndrome.

Secondary syphilitic icterus would appear to belong to the class of hæmolytic icteri, according to recent researches, particularly those of Gaucher and Giroux.

Secondary Syphilitic Nephritis, apart from any former renal taint, generally occurs in the third and eighth month of syphilis. It is revealed most frequently by sudden and considerable dropsy, and by albuminuria, which frequently reaches 10 to 15 grammes daily, sometimes even 50 grammes. More or less pronounced signs of uræmia may accompany the dropsy: vomiting, headache, etc. Recovery is the rule, provided the patient is energetically treated, and as soon as possible after the beginning of the disease; it is often slow, and the albuminuria may persist for several months.

Finally, I must mention **Phlebitis,** which is frequent during the secondary period and often coincides with the roseola. It affects the superficial veins of the lower limbs, and nearly always several of them simultaneously, often those of both legs. It is characterised by the development of hard cords, neither voluminous nor painful, often indeed painless, and never gives rise to œdema or embolism.

GENERALITIES OF TERTIARY SYPHILIS

There is no necessity to describe the tertiary lesions of syphilis; they are met with relatively seldom in military practice, and have no special indications, apart from the question, not without importance, of the invaliding they may bring about. Their treatment offers no particular indication, beyond the necessity, always important in the army, of carrying out as

actively as possible the cure of soldiers who, after recovery, may be again sent to their unit. Although certain localisations of tertiary syphilis may be contagious, this is so exceptional that there is never any necessity to send a tertiary syphilitic to hospital when the lesions by which he is affected do not interfere with the performance of his military duty, or do not necessitate energetic treatment incompatible with the obligations of service.

I must insist upon this last point, because I have too frequently seen men sent to hospital who were suffering from tertiary lesions of the skin or tongue, neither ulcerated nor painful, which did not in any way prevent them from carrying out their duties, and only required treatment which could easily be carried out with the unit. Men often take advantage of their disease to impose on the medical man.

I shall only briefly summarise the principal localisations of tertiary syphilis.

As regards the skin, syphilides of various types are observed, papular, papulo-tubercular, ulcerous, gummatous, always characterised by : (1) their form, which is nearly always round, or reniform, and their disposition in groups of more or less rounded configuration, and by centrifugal extension when they are multiple ; (2) the small number of their elements, and their habitual limitation to one region of the body or to a small number of regions, contrary to secondary syphilides, which are usually generalised ; (3) the tendency to ulceration, or, if they do not ulcerate, to interstitial absorption of the invaded tissues ; hence the usual persistence of indelible cicatrices, often, but not always, surrounded by a zone of pigmentation ; (4) the absence of functional phenomena, pruritus, and pain, except when there is ulceration, and often even when they are situated in the neighbourhood of orifices and in very mobile regions.

The diagnosis of tertiary syphilitic lesions rests on

these characteristics: on the former existence of recognised syphilitic affections (it must be borne in mind that syphilitic antecedents are frequently absent, less often, however, in a man than a woman), on the verification of syphilitic stigmata, cutaneous cicatrices, Argyll Robertson sign, abolition of the tendon reflexes, on the existence of a positive Wassermann Reaction; in doubtful cases, rapid recovery by mercurial, arsenical, or iodide treatment may settle the diagnosis.

The most frequent lesions of the accessible mucous membranes are ulcerations and sclero-gummatous lesions of the tongue, with or without leucoplakia, or at least certain of its forms, for it would be, at the present time, excessive to state that leucoplakia is always caused by syphilis; ulcerous lesions of the soft palate, leading generally to rapid perforation, and which it is necessary to treat very actively from the beginning.

The visceral, arterial, cardiac, nervous, hepatic, and other lesions, which constitute an important part of internal pathology, need not be described here.

CHAPTER V

TREATMENT OF SYPHILIS

THE SPECIAL CONDITIONS OF THE TREATMENT OF SYPHILIS IN THE ARMY

The anti-syphilitic medicaments may be reduced to three substances—mercury, iodine, arsenic; but the methods of administration and the preparations of these three substances are numerous. Each syphilologist has made a choice amongst these preparations, and laid down special rules for their application, which seem to him to respond best to the therapeutic indications of syphilis. Thus, he has evolved an elective type of syphilitic treatment which he habitually employs; but, if he has the medical spirit, he knows how to deviate from this type and modify it, according to the indications of each case, as well as to the social condition of the patients.

The conditions of military life, more especially those of the present war, introduce special indications and choice of treatment, which military surgeons and syphilologists must take into account. In default of this adaptation to military conditions, the doctor will meet with great difficulties, sometimes the formal opposition of the staff to the execution of the treatment he prescribes: indeed, he may cause a useless reduction of effectives and cripple the necessities of national defence.

Let us first consider the special indications in the army during the present war.

In the case of combatant soldiers at the Front, men remaining at the depots, or employed in the interior, especially men in munition works, attacked by a contagious disease of any kind, it is necessary, in the first place, to put them out of the way of doing harm to others by transmission of their disease. On the other hand, they must be rendered fit for service in their companies or workshops as soon as possible, and the evil effects resulting from their disease must be re-reduced to a minimum.

In the case of syphilis, these necessities indicate two precepts :

(1) Cause the disappearance, by the most energetic treatment possible of contagious lesions, which, fortunately, develop on surfaces accessible to direct examination, and may, consequently, be recognised and watched.

(2) When the contagious lesions are healed, the treatment should be continued, less energetically than at first, but sufficiently to protect the man from later contagious lesions and the different manifestations of the disease, by processes which do not hinder his military duties from being carried out.

Certainly, the problem would be solved in its entirety, if one knew of a sure and rapid method of sterilising syphilis by medicamental or biotherapeutic treatment. Despite the somewhat incautious pretensions held out by Ehrlich on the action of arsenobenzol, the problem has not been solved ; I shall show later what one must think about this subject.

We must, therefore, content ourselves with the measures at our disposal to do the best we can, under somewhat contradictory conditions, to deal with the problem of the treatment of syphilis in the Army.

In order to determine these measures and their application, it is necessary to find out what can be

expected of the different antisyphilitic agents and their various modes of employment.

I will first of all eliminate iodine and its different compounds, iodide of potassium and of sodium, tincture of iodine, organic preparations of iodine, etc. All these agents have their proper place in the antisyphilitic arsenal; but, with the exception of mercurial iodides, which will be studied with the mercurial compounds, their place is in the background. They are almost entirely without action on the sterilisation of syphilis, on its first manifestations, or its various contagious lesions, and, in any case, cannot be considered in the primary or secondary periods, either as active agents of treatment or as having a prophylactic action on subsequent complications. It is during the course of the tertiary manifestations that they have a real value in the treatment of gummatous or ulcero-gummatous syphilides of the skin and mucous membranes, or on the cardio-vascular lesions, so common in syphilis. But tertiary lesions are beyond the scope of this study.

There remain, then, mercury and arsenic.

MERCURY

As regards syphilitic therapy in the Army, there is one point of great importance. This is the mode of administration of medicaments.

The conditions for supplying bodies of troops and medical centres with drugs, for distributing these to the patients, and, in the case of prolonged treatment for which the soldier cannot present himself daily at the hospital, the necessity of his being able to take his supply of drugs with him; the advantage there is in men, and especially officers, being treated in more or less secrecy, are some of the principal considerations which must guide the military surgeon in his selection of the method of treatment—apart from the special action and form of the drugs.

I shall, therefore, consider successively :

(1) Mercurial medication by ingestion (solution, syrups, pills, tabloids, cachets) ;

(2) Mercurial medication per rectum (suppositories) ;

(3) So-called endermic mercurial medication (rubbings) ;

(4) Intramuscular mercurial medication (injections of soluble and insoluble preparations) ;

(5) Intravenous mercurial medication.

Mercurial Medication by Ingestion

(*a*) **Solutions and Syrups.**—These two pharmaceutical forms are absolutely inapplicable at the front, by reason of the difficulties there would be in supplying the regimental hospitals, and the impossibility of transporting the liquids.

In medical centres in the interior there would still be the inconvenience of manipulation of large quantities of liquids.

Although the absorption of a drug in solution is more regular than in the form of pills, these or tabloids completely replace the solutions.

However, in some cases—especially of tertiary lesions, which are rarely observed in the Army and are beyond the scope of this study—van Swieten's * Liquor in small doses, according to Brocq's method (five cubic centimetres administered four to six times daily) is better than treatment by pills.

With regard to mercurial syrups, of whatever kind, there is no reason to use them in the Army. Gibert's syrup, the best known and most used among them, is a bad preparation, often causing gastralgia ; its dosage in iodide of potassium is insufficient for

* Van Swieten's Liquor, a solution of sublimate in a thousandth part, is given in the *Formulaire pharmaceutique des hôpitaux militaires*, and the preparation is prescribed without alcohol.

carrying out mixed treatment with iodide and mercury.*

(*b*) **Pills, tabloids, cachets.**—For a long time, pills have been the form in which drugs are most used in the treatment of syphilis : " Treatment, easy to carry out in secret, even when travelling," according to the well-known formula.

They have the great advantage of being easily taken about and of keeping a fairly long time, and are consequently capable of being stocked in all hospitals and medical centres. They can be given to men for continuous and prolonged treatment without obliging them to report frequently to the doctor. They must be well prepared, the pill mass should be soft, with a sufficient quantity of glycerine added to prevent desiccation. When hard as stones, as they are sometimes, they pass through the digestive tract undissolved and are rejected without doing more than simulate treatment.

The *Formulaire pharmaceutique des hôpitaux militaires* mentions no other mercurial pills, except those of protoiodide of mercury.

The formula is as follows :

Protoiodide of mercury	2 gr. 50
Powdered opium	1 ,,
Powdered liquorice	2 ,,
Extract of juniper	*Q.s.*

D. in 100 pills.

Each pill contains 25 milligrammes of protoiodide of mercury, a very judicious dosage, which enables the

* Gibert's Syrup is given in the *Formulaire pharmaceutique des hôpitaux militaires* under the name of mercuric iodide. Its composition is as follows :

Mercuric iodide	1 gr.
Iodide of potassium	50 ,,
Distilled water	50 ,,
Simple syrup	900 ,,

Therefore, per 20 gr. it contains a centigramme of mercuric iodide and 50 centigrammes of iodide of potassium.

daily dose to be graduated according to the tolerance of the patients, and far preferable to the dosage of 5 centigrammes in Ricord's pills.

The difficulty of this formula is to supply pills which dissolve easily when they have been prepared a certain time. Medical men must, therefore, be careful to renew their supplies at sufficiently short intervals, without waiting for the period of quarterly supply for drugs.

When patients wish to pay themselves for their supply of protoiodide pills, it will be better to give them the following prescription for a *soft* pill :

Protoiodide of mercury	25 mgr.
Extract of thebaine	1 cgr.
Glycerine excipient	*Q.s.*

Protoiodide of mercury is, *par excellence*, the drug for secondary syphilis : its renown for this period is universal. It has the advantage of being tolerated by the stomach, but produces salivation more easily than sublimate.

The usual dose of protoiodide to be prescribed daily is 10 centigrammes ; this represents four pills to be taken four times daily, after meals.

Certain patients cannot tolerate protoiodide well, in which case another mercurial salt must be given. The best is sublimate, the basis of Dupuytren's famous pills.

Sublimate pills do not figure in the *Formulaire des hôpitaux militaires*, and so are not supplied in quantities to regimental hospitals : they can only be made up in medical centres provided with a chemist, or from prescriptions made up by a civil chemist.

The simplest formula is the following :

Corrosive sublimate	*aa.* one centigramme
Extract of thebaine	
Glycerine excipient	*Q.s.*

for a *soft* pill.

Usual daily dose: 2 pills, *i.e.* 2 centigrammes of sublimate.

Sublimate is generally tolerated well by the gums, but often causes gastric pains or diarrhœa; it may be useful then to increase the dose of extract of thebaine in the pills.

Compressed tabloids are used too rarely for the administration of mercury. They have the advantage of pills, in dissolving easily and completely.

The Central Pharmacy for Military Hospitals supplies tabloids containing 0·025 gr. of protoiodide of mercury for the use of regimental infirmaries and medical centres, which can be used in the place of pills. I believe that these tabloids are now being supplied.

Cachets are rarely employed as a medium for the administration of mercury. A few years ago, Alex. Renault recommended them for this purpose, and they constitute an improvement on mercurial pills: the rapid and complete absorption of the drug is assured by this form, which can be easily transported and only necessitates more careful packing.

Mercurial cachets are not entered in the nomenclature of drugs supplied by the Central Pharmacy for Military Hospitals.

All men in a position to bear the expense, especially officers, who prefer them to pills because they are less compromising, can procure them at their own cost.

Protoiodide of mercury is the only mercurial salt suitable for administration in cachets; if sublimate were introduced undissolved into the stomach there would be a risk of causing erosions or chemical ulcerations; calomel is unsuitable, owing to its somewhat irregular action, and its transformation into sublimate under the influence of certain foods.

The following is Alex. Renault's formula for cachets:

Protoiodide of mercury	5 cgr.
Powdered opium	1 or 2 cgr.
Powdered cinchona	*Q.s.*

to fill a small 25 centigrammes cachet.

He prescribes 4 per day, *i.e.* 20 centigrammes of protoiodide of mercury.

I prefer using cachets with a dosage of half the quantity, *i.e.* 25 milligrammes of protoiodide, and not to exceed the daily amount of 10 centigrammes of this salt.

The various modes of administration of mercury by the mouth, together with mercurial inunction, were for a long time the only means of treating syphilis.

Although they have a real action on syphilis, and especially on secondary troubles, it is acknowledged that this action is weak and in no way comparable to that of the drugs which will be considered later on.

They cannot in any way be used to attack the disease at its onset, bring about the abrupt cicatrisation of chancre, or the rapid cure of mucous plaques.

They must, therefore, never enter into the initial treatment of syphilis, in the intensive treatment given in hospital for sterilising contagious symptoms.

But they have a real value as a means of continuous and prolonged mercurialisation, after cure of the contagious troubles, as a means of maintaining treatment by Fournier's "intermittent cure."

As men can carry them easily, or renew their stock when exhausted, pills, tabloids, and cachets should be prescribed for them when they are leaving the hospital, after they have been subjected to intensive treatment, and when they require treatment for some non-contagious manifestation, compatible with the continuation of their military service.

If the various ways of buccal mercurial administration have the advantage of avoiding the necessity of the patient's frequent visits to the doctor, they have, on the other hand, the disadvantage of removing him from direct medical supervision. Here, it is necessary to rely on the patient to attend to himself regularly. The doctor must warn him not to neglect the ingestion of the pills or cachets.

With regard to the general cure of syphilis, I shall indicate the progress of treatment by pills later (see page 146).

Mercurial Medication per Rectum

Rectal mercurial medication by means of suppositories is but rarely used, too seldom in fact.

Recommended by Charles Audry (Toulouse) it is well borne, and but rarely gives rise to local trouble ; it has the great advantage of protecting the upper digestive tracts in patients, numerous amongst colonial troops, whose stomach and small intestine cannot tolerate mercury administered by ingestion. With these patients, as with gastropaths in general, it replaces subcutaneous and intramuscular injections of mercury which, as we shall see, are not often applicable to syphilis in the army.

Mercurial suppositories cannot be kept as long as pills, necessitate more careful preparation, much more complicated packing, take up a little more room, are more expensive than pills, and finally are not included in the Pharmaceutical Formulary for Military Hospitals; so that they can only be used by soldiers under treatment in certain medical centres, or who are able to buy them.

Their indications are almost similar to those of mercurial cachets, with this difference that they are suitable for patients suffering from lesions or gastric troubles, but their use is not always compatible with the promiscuousness of camp life.

It would be well, however, under suitable conditions, to employ them more largely than has hitherto been the case, especially for officers, and I have sometimes found them beneficial.

Audry * recommends suppositories prepared with

* Ch. Audry: "Preliminary note on the administration of mercury per rectum," *Annales de dermatologie*, October 9th, 1905, p. 703; "Treatment of syphilis per rectum," *Annales de dermatologie*, March 1906, p. 231.

40% grey oil. The daily dose of metallic mercury suitable for the treatment of syphilis in an adult per rectum being 3 centigrammes, the suppositories are prepared in the following way :

Grey oil, 40%	gr. 0·075
Cacao butter	4 gr.

Melt the cacao butter, let it cool again, and when it begins to lose its transparency mix rapidly with the grey oil and pour into the mould.

Endermic Administration

Mercurial inunction, for long the classical process, is to-day practically abandoned. This is not the place to discuss whether it should be re-established. Indeed, it appears to me to be completely useless in army practice. The difficulty the men would have in carrying it out in camp, the impossibility of their taking baths, the dirtiness of mercurial ointment and soiling of their clothes prohibit its employment in the army zone. In the medical centres the difficulties are almost the same, and inexperienced orderlies are often entrusted with the rubbings, which require a certain amount of practice to be done well, and are liable to cause severe stomatitis.

Moreover, whatever one's opinion may be of the therapeutic value of mercurial inunction, it is unsuitable both for the intensive treatment at the onset of syphilis and the continuation of treatment afterwards, and, even in times of peace, its indications are limited.

Intramuscular Administration of Mercury *

Two series of mercurial preparations may serve for the intramuscular treatment of syphilis ; the one

* I say intentionally intramuscular and not subcutaneous, because I consider that all mercurial injections, whether of soluble or insoluble preparations, should be made into the muscle, and not in the subcutaneous tissue as some authors advise.

insoluble, the other soluble. The frequency of the injections, their effects, and administration differ essentially, according to which series is employed.*

(*a*) **Injections of Insoluble Preparations.**—Insoluble mercurial injections have the *advantage* of introducing into the muscular tissue a relatively large quantity of mercury which, under the influence of chemical reactions produced by substances in solution in the blood and plasma, dissolve gradually and, by therapeutic action taking place at regular intervals, really constitute a continuous and regular treatment. The mercurial reserve deposited in the muscles is calculated in such a way that its solution and absorption are sufficiently advanced at the moment the next injection is given.

In practice, the injections are made at intervals of a week, which enables the patient to regulate his visits to the doctor.

As a corollary to this advantage, there is the *inconvenience*, more theoretical than real, of exposing the patient to an overdose of mercury, when the solution of the mercury is too rapid.

If certain rules are ignored, the injections might cause the deposit of too large a quantity of mercury in the tissues; the patient could not be relieved of this surplus of mercury, or only with difficulty by surgical intervention, if the phenomena of mercurial intoxication developed; hence the possibility of grave accidents, even death.

As a matter of fact, the dangers of insoluble mercurial injections, of which some medical men have unjustly made a scare, are practically non-existent: in all, or nearly all, the fatal cases, reported in their

* Some soldiers may be tempted, on account of the pain, to escape treatment by intramuscular or intravenous injections. A judgment of the War Council, dated September 7th, 1916, condemned a soldier to three months' imprisonment for having refused to submit to an intramuscular injection prescribed by the medical man in attendance.

entirety, some error is revealed : the doses of mercury have been too high, the injections too close together, and, above all, these have been continued when signs of mercurial intoxication, especially stomatitis, have already appeared. These phenomena should have caused the suspension of the injections.

These accidents have been observed specially with grey oil. Now, for twenty-five years I have made, or caused to be made, more than 60,000 injections of grey oil and have only seen two of my patients succumb. In one of these the injections had been continued by error, after the appearance of stomatitis. The other died after the untimely extraction of twelve or fourteen dental stumps at one sitting, during the course of treatment, which was followed by extensive necrosis of the jaw.

A more justifiable objection may be raised to insoluble intramuscular injections—the pain they sometimes cause. This is often severe after injections of calomel, but is generally absent after injections of grey oil, provided it is well prepared and a sufficiently fine needle is used. Nevertheless, pain may be produced after piercing a nervous filament, and, as the injection is made in the gluteal muscles, this may impede walking. Sometimes the pain following injections of grey oil may result from the development of an inflammatory nodule in the subcutaneous cellular tissue or in the muscle ; it then appears on the third or fourth day and subsides in about a week. It is altogether exceptional for the nodules to suppurate, and, when suppuration appears, spontaneous opening or an incision results in rapid recovery.

The sole possibility of pain, of the unfitness of the man—pain which may be more or less real, which some soldiers may exaggerate and even make a pretext for discharge from duty—suffices to show that insoluble injections cannot be used in the treatment of syphilis at the Front.

Grey oil has an activity inferior to that of cyanide of mercury in intravenous injections, but equal or superior to that of the majority of soluble intramuscular injections ; it is of very practical use in the *continuation of treatment.* The injections, made in doses which will be indicated later on, once a week in a series of six to eight, every three or four months, constitute sufficient medication, after intensive treatment at the onset. The doctor is sure an injection has been made, he is not always sure that a pill has been taken and swallowed; neither he nor the patient is too busy for a weekly injection.

Calomel in intramuscular injections is one of the most active mercurial preparations ; it is specially indicated in refractory localisations of tertiary syphilis in the tongue or brain. But the injection often causes acute pain ; appearing on the third or fourth day, it reaches its maximum on the fifth or sixth, and is often sufficient to prevent the patient walking. It persists for three or four days, leaving behind it painfulness in the gluteal region.

Injections of basic *salicylate of mercury* and *yellow oxide of mercury*, less used than calomel, have the same inconveniences.

Finally, these three preparations, as well as grey oil, are not suitable for the treatment of syphilis at the Front. They may be employed in medical centres, on patients suffering from grave lesions, removed from active service for some time by illness or wounds.

The grey oil mentioned in the *Formulaire pharmaceutique des hôpitaux militaires* is that of the Codex, containing 40% of mercury ; 100 cubic centimetres contain :

Purified mercury	40 gr.
Sterilised anhydrous lanoline	26 ,,
Sterilised oil of vaseline . . .	about 60 ,,

Prepared with the necessary care, on which I need

not insist here, it should be homogeneous in appearance. and, under the microscope, only reveal minute grains of mercury.

The weekly injection of grey oil is made with a dose of seven to eight centigrammes of mercury, which corresponds to three and a half or four divisions of a Pravaz syringe of one cubic centimetre capacity. When making injections of grey oil, it is necessary to use very accurately marked syringes ; the rod of the piston should have an index, so as to avoid the correct dose being exceeded.

Calomel oil appears in the *Formulaire pharmaceutique des hôpitaux militaires* with the following composition :

Calomel	5 gr.
Sterilised anhydrous lanoline	16 ,,
Sterilised vaseline oil	100 ccm.

I prefer the following formula, which causes less pain :

Calomel washed in alcohol . . .	5 or 10 gr.
Sterilised sweet oil of almonds . .	100 gr.

The oil should be thoroughly shaken before being introduced into the syringe.

The quantity of liquid injected must be calculated in such a way as to introduce 5 to 10 centigrammes of calomel into the muscle.

The injections are repeated once a week, not exceeding four or six injections in a series.

Insoluble injections must be made in the muscle, with the precautions which will be indicated later when describing the technique of intramuscular injections (see p. 607).

(*b*) **Injections of Soluble Preparations.**—Numerous soluble mercurial preparations have been proposed for the treatment of syphilis by means of injections. A few only, which I shall enumerate farther on, have

been retained, owing to their activity and tolerance by the tissues.

In a general way, the activity of these preparations does not vary very considerably from one to another, on condition that they are employed in comparable doses. This activity is inferior, on the one hand, to that of intravenous injections, and, on the other, to that of calomel injections. It is still more inferior to that of arsenical preparations.

Therefore it is impossible, with any of these soluble preparations, to carry out the intensive cure of syphilis, which, at the present time, is a strict obligation at the period of chancre or of secondary symptoms. I myself have seen too many syphilitics who, after being in hospital for a chancre for two or three months, and having received from forty to ninety soluble mercurial injections during this time, have hardly been discharged before they are admitted to another hospital with an eruption of generalised syphilides, or a crop of mucous plaques on the mouth.

Soluble intramuscular injections have the advantage over insoluble injections of not exposing the patient to the danger of mercurial accumulation. I have already shown that these dangers are in reality very small with a careful technique.

They are not often painful, but here again distinction must be made between the preparations: those which have the reputation of being painless, like mercuric benzoate, are painful if the needle touches a nerve; they may even, if not injected deeply and with care, produce nodules and abscesses, which are often very painful.

Compared with injections of insoluble preparations, those of soluble preparations have the disadvantage of requiring the patient to attend for treatment three to six times a week, whereas an injection of grey oil is only made once a week.

In short, intramuscular injections of soluble prepara-

tions are unsuitable for the intensive treatment of syphilis, and in later treatment they require too frequent visits to the doctor. The pain they may cause, moreover, renders them unsuitable for men engaged in active service, especially those who are serving at the Front.

Hence, their applications in war practice are very limited ; they are reduced to the treatment of syphilitics who, in hospital for some cause, apart from syphilis, nevertheless require mercurial treatment more active than by pills, or those who do not tolerate these, or men whose veins are not prominent enough for intravenous injections.

The solutions for intramuscular injections, given in the *Formulaire pharmaceutique des hôpitaux militaires*, are the following :

(1) *Solution of benzoate of mercury.*

Benzoate of mercury	1 gr.
Pure chloride of sodium	0·75 gr.
Sterilised distilled water	100 ccm.

This solution contains 1 centigramme of benzoate of mercury per cubic centimetre.

It is injected in a dose of 1 cubic centimetre daily or every other day.

(2) *Aqueous solution of biniodide of mercury.*

Biniodide of mercury	0·50 gr.
Iodide of sodium	0·50 gr.
Neutral phosphate of sodium	1 gr.
Pure chloride of sodium	0·35 gr.
Sterilised distilled water	50 ccm.

This solution contains one centigramme of biniodide of mercury per cubic centimetre, corresponding to 0·044 gr. of metallic mercury.

(3) *Oily injection of biniodide of mercury.*

Iodide of mercury	0·20 gr.
Guaiacol	0·10 gr.
Purified and distilled olive oil	46 gr.

Cyanide of mercury, which has been recommended, has to be discarded, owing to the pain caused by its injection into the tissues.

Oxycyanide of mercury in an isotonic solution, or with the addition of its weight in stovaine, is not painful. It is injected in a dose of 1 centigramme.

Neutral salicylate of mercury in an aqueous 2% solution is well tolerated.

Technique of Intramuscular Injections. — Intramuscular injections must be made with needles of sufficient length to reach the muscular tissue, *i.e.* 4 to 5 centimetres. I specially recommend that steel needles should be used, as they pierce better than platinum ones, and, for the same inside calibre, have a smaller external diameter than the latter. This last point is of importance for injection of grey oil; it often happens that, when the needle is withdrawn, a certain quantity of the liquid injected runs back along the track; the larger the passage left by the needle, the greater this reflux, and the more chance is there of its going into the cellular tissue. Now, it is the penetration of grey oil into the superficial fascia which causes the formation of subcutaneous nodules after injections. Another reason has caused me to discard platinum needles: these are manufactured by rolling and soldering a platinum plate, and are often perforated after a certain number of sterilisations in the flame; the result is that a small drop of grey oil may escape through one of these perforations, penetrate into the cellular tissue and cause the development of a nodule there, or in the dermis, thus producing an eschar which takes a long time to heal.

Intramuscular injections of preparations dissolved in water can be made almost without inconvenience in the buttock; care must be taken, however, to avoid the neighbourhood of the sciatic notch. This precaution is still more necessary with injections of insoluble preparations; the penetration of fluid into the

vessels which run through the sciatic notch might give rise to embolism and cause death.

In order to avoid this dangerous zone and, if nodules do develop, to prevent their inconveniencing walking or dorsal decubitus, the injections should be made in an area the width of two fingers in height and of three fingers in width, the external border of which is 3 centimetres behind the great trochanter and the lower border 2 centimetres above the lower border of the trochanter ; or in the upper third of the buttock.

When an oily fluid is injected, or insoluble substances are held in suspension, I cannot warn too strongly that the injection should never be made without the needle having first been introduced alone, to be sure that no blood appears, the flow of blood indicating penetration of a vessel.

The Intravenous Administration of Mercury

Baccelli introduced intravenous injection for the administration of a certain number of drugs. It was employed by Abadie for the treatment of ocular syphilis, and entered into the practice of syphilologists long before colloidal substances were used in general medicine.

The only mercurial salt commonly used in syphilis is *cyanide of mercury*. The number of mercurial compounds suitable for intravenous injection is singularly restricted by the conditions to be fulfilled. These are as follows : the drug must be soluble, stable, have a fixed and determined mercurial content, be easily prepared, sterilisable, and, finally, must not precipitate the blood albuminoids.

Now, cyanide of mercury practically fulfils all these conditions. The radical cyanogen is, as it were, dissimulated in the same way as arsenic in organic arsenical compounds and, from the point of view of toxicity, no relation can be established between it and cyanide of potassium.

Aqueous solution of biniodide, which has been recommended by some authors, has not been admitted into current practice.

The *advantages* of intravenous injections are multiple: complete absence of pain when the injection is made correctly; rapid absorption and elimination of the mercury which, at the end of an hour, appears in the urine, presenting its maximum at the end of three to six hours, hence the absence of accumulative effects and the possibility of renewing the injections at short intervals; total absorption, and absence of all cause of error in dosage; finally, rapid and energetic therapeutic action. I shall refer to this point again later.

The *inconveniences* and *accidents* are real, but may be nearly always avoided, given good technique. They consist in the possible introduction of the fluid into the wall of the vein and subcutaneous cellular tissue, with resulting venous indurations and dermo-hypodermic eschars; in the action of the drug on the digestive tube, with dysenteriform and hæmorrhagic colitis. Seeing the importance of the question of the technique of intravenous injections in general in the treatment of syphilis, I have grouped together in a special chapter all that concerns technique, injection accidents and the means of preventing such accidents (see p. 650).

An objection raised with regard to intravenous injections is the complicated and difficult technique: I repeat that with a very small amount of skill and attention every medical man should soon learn how to make an intravenous injection correctly. In hospital, my pupils succeed at the end of a few days in acquiring sufficient dexterity. For several months many military surgeons have come to my clinic to learn the operative technique of intravenous injections, and have been able to perform these perfectly after two or three days at the most.

Another objection raised to intravenous injections

is the time they require ; it is certain that, in a doctor's practice, an intravenous injection and its preparation demand an appreciable time ; but this does not sensibly exceed that taken by an intramuscular injection and its preparation. In a hospital treating a number of syphilitics and provided with a staff of well-trained dressers, the time of preparation is distributed amongst the total number of patients ; it is reduced in proportion to the number of injections made at the same sitting, and what might be termed the therapeutic yield becomes considerable.

As against the inconveniences, one must put *the therapeutic value* of intravenous injections of cyanide of mercury. This value, I can say without hesitation, is enormous and superior to that of all other forms of mercurialisation ; it can only be compared to that of injections of calomel in tertiary syphilitic lesions of the mucous membranes.

It is not rare to see syphilitic chancres dating from eight to ten days cicatrise after two or three intravenous injections of cyanide of mercury ; syphilitic lesions of all sites, secondary or tertiary, mucous plaques of the pharynx, hypertrophic cutaneous syphilides become cicatrised or healed in a few days. One cannot pretend that these results are constant, and I have seen syphilitic lesions resist this mode of treatment ; I consider that, when a series of ten to twelve intravenous injections of cyanide of mercury has not effected the cure of the syphilitic lesion, it is not worth while continuing this treatment and better to have recourse to another.

It is none the less true that in the generality of cases, especially primary and secondary lesions, intravenous injections constitute a very active treatment, an *attacking treatment* for which no mercurial preparation, and above all *no mercurial preparation* suited for the treatment of syphilis in soldiers, *can be substituted*. I shall show later the practice I have devised for the

purpose of associating intravenous injections of mercury and those of novarsenobenzol.

Intravenous injections of cyanide of mercury are made with a 1 % solution of this salt in sterilised distilled water.

In the centres where injections of cyanide of mercury are of current use, this solution may be kept in glass-stoppered bottles; they must be replaced every two or three days.

When there is only a small consumption of cyanide, the provision must be kept in sealed ampoules of 1 or 2 cubic centimetres capacity.

The injections are repeated every day, or every two days, according to the rapidity with which the treatment is to be carried out. They may be given daily without inconvenience for twelve to fifteen days; but must be suspended if they produce either stomatitis, which is rare, colitis, or hæmorrhagic stools, which are more frequent.

The ordinary dose of cyanide to be injected at one time is 1 centigramme, say 1 cubic centimetre of the 1 % solution. It is prudent to commence with an injection of 5 milligrammes only, say a half cubic centimetre, in debilitated or aged subjects, or in those in whom intestinal troubles are suspected; but if the first injection is tolerated well, the normal dose of one centigramme may be given after the second or third injection.

When it is necessary to push the treatment very actively, for example, in patients whose military duties do not permit more than a short sojourn in hospital, or when one has to deal with grave syphilitic lesions, such as iritis, meningitis, etc., two centigrammes of cyanide (*i.e.* two cubic centimetres) may be injected every day, or one day out of two, in which case there should be an injection of one centigramme on the intermediate days.

In a word, the medical man must vary the doses

according to the indications given by each patient from day to day.

ARSENIC

For some considerable time arsenic has been used in the treatment of syphilis, as an accessory medication. Donovan's solution, which dates from 1839, contains it in association with iodide of potassium and mercury; numerous medical men add arsenic, either to mercury or iodide of potassium, and use it for combating the anæmia and asthenia of syphilitics, or prescribe thermal baths for these patients, where the waters contain arsenic, especially at Bourboule.

From the time that Armand Gautier introduced arsenical derivatives with an organic base into therapeutics, these have been employed largely in antisyphilitic therapy. Brocq obtained good results with iodo-mercuric cacodylate; arrhenate of mercury, salicylarsenate of mercury have been used. Anilarsinate of sodium, which was discovered by Béchamp in 1863, reappeared in Germany in 1907, under the name of atoxyl, and enjoyed an ephemeral vogue, but was soon abandoned owing to the numerous and serious accidents it caused (blindness, death).

In 1909, Balzer obtained good results with *benzo-sulphono-para-amidophenylarsinate of sodium*, discovererd by Mouneyrat and sold under the name of hectine; associated with mercury in a special preparation, under the name of hectargyre, it had a certain vogue, which rapidly diminished upon the appearance of arsenobenzol.

Arsenobenzol

Dichlorhydrate of dioxydiamido-arsenobenzol was discovered by Ehrlich, in 1909, when experimenting with arsenical compounds on the spirilloses. It is commonly

known by the name of "606," which indicates its number in the series of Ehrlich's experiments. It has been patented under the name of Salvarsan by the Hoechst Chemical Manufacturing Dye-works of Meister Lucius, and Brüning. The name *arsenobenzol*, a simplification of its chemical denomination, under which it has been manufactured and sold everywhere, should be the only one used.

Arsenobenzol is a canary yellow powder, impalpable to the touch, of an astringent and acid taste, with a slightly sulphurous odour; it changes under contact with the air, and must be kept in hermetically sealed phials, in nitrogen.

In water, it gives a solution, with an acid reaction.

It was at first used for intramuscular injections, in the form of an acid oily suspension, but this method of employment was soon abandoned owing to the severe pain it caused. Arsenobenzol was then administered solely by intravenous injection: its aqueous solution, being acid, has been abandoned, on account of the painful reactions it caused; recourse has been had to neutralised solutions, or those rendered alkaline by the addition of solution of soda.

The quantity of solution of soda to be added varies in accordance with the doses injected.

The addition of solution of soda to the aqueous solution of arsenobenzol produces a precipitate, which dissolves on the addition of more alkaline solution.

Arsenobenzol solution, rendered alkaline by soda, cannot be injected unless diluted by a certain quantity of physiological serum, so that the volume injected shall reach 150 to 200 cubic centimetres.

Each operator prefers his special method, the preparation of the solution, and the instruments necessary for the injection having been subjected to numerous modifications. It is not possible here to give details of these different techniques, the more so because, as I shall state later on, I do not consider arsenobenzol

can be utilised in the treatment of syphilis in the Army.

When first used, arsenobenzol gave rise to the greatest hopes. Ehrlich did not hesitate to say that it enables one to effect, by means of a few injections, the "sterilisatio magna" of syphilis. Experience quickly showed that, even granting that these injections given at the onset of syphilis were indeed followed in a short time by cicatrisation of the chancre, if the secondary symptoms did not appear at their ordinary date, they were simply delayed and were frequently seen later. In an attempt to stop the secondary symptoms, it was necessary to increase the number of injections. True, when the disease was more advanced, active troubles certainly disappeared, most frequently in a marvellous way, but these also reappeared at the end of some weeks, and sometimes then resisted arsenobenzol, even in large doses frequently repeated.

Thus the initial enthusiasm was damped; injections were multiplied, and doses increased.

Moreover, accidents happened, even deaths being reported. Many of these accidents were due to errors of technique or the use of excessive doses and could not be attributed to the drug. As regards the deaths, the majority were due to the general condition of the patients. Ehrlich soon announced that there were contra-indications to the use of arsenobenzol, and advised its non-employment in cardiac affections, aortic aneurisms, and general paralysis.

Nevertheless, disastrous results were still observed sometimes; it had to be acknowledged that, granting they were more frequent in old age, and in cardiac, albuminuric, hepatic, and cachectic patients, they were also observed in young, apparently healthy subjects. It was soon noticed that they rarely appeared with the first injection, but most often with the second, diminishing in frequency with the third and subsequent ones.

Further, nervous troubles such as paralysis of the cranial nerves sometimes appeared in patients treated by arsenobenzol ; their frequency aroused distrust of the drug

I shall revert again later to the question of accidents.

Arsenobenzol caused accidents, independent of the doses of the drug injected, as well as of the technique ; it necessitated a complicated technique, and, despite improvements, few medical men were persuaded to use it.

The discovery by Ehrlich of a substance, of closely allied chemical composition, easily giving a perfect solution with neutral reaction, rendered the arsenical medication of syphilis practicable.

Novarsenobenzol

Dioxydiamido arsenobenzolmonomethylene sulphoxylate of sodium was called " 914 " by Ehrlich, in accordance with its position in his experiments ; it was sold by the firm of Meister, Lucius, and Brüning, under the name of Neosalvarsan. By way of analogy with arsenobenzol, it is generally designated under the name of *Novarsenobenzol.* Like arsenobenzol, it can be prepared and sold by all manufacturers of chemical products.

It is a bright yellow * powder, of impalpable consistency ; when placed on water it floats, but melts with extreme rapidity, making a clear solution, of neutral reaction, which can be injected into the veins direct.

The perfect and rapid solubility of novarsenobenzol in water in every proportion, or in physiological serum,

* When novarsenobenzol changes, its colour becomes brown. Before making the solution, care should always be taken to see that the product has retained its normal colour. It is well to know that the density of novarsenobenzol is not always constant, so that the volume in the ampulla occupied by the same dose of the drug may vary considerably.

has caused this substance to obtain a well-merited renown.

Novarsenobenzol changes rapidly when in contact with the air : like arsenobenzol, it must also be preserved in hermetically sealed ampoules. This is the form in which it is put on the market and delivered to medical centres, by the Central Pharmacy of Military Hospitals and the local pharmacies, in ampoules containing doses of 0·15 gr., 0·30 gr., 0·45 gr., 0·60 gr., 0·75 gr., 0·90 gr., the doses usually employed for the treatment of syphilis. The ampoules have a uniform capacity of 4 to 5 cubic centimetres.

The activity of novarsenobenzol is lower than that of arsenobenzol ; both from the point of view of toxicity and of therapeutic effects, it may be regarded as equal to two-thirds of that of arsenobenzol. Thus, the doses should be half as much again as those of the latter drug.

Novarsenobenzol solution should be prepared the moment it is to be used ; its effect changes on contact with the air, and this becomes more accelerated the higher the temperature. Further, these solutions should be used with *cold water*.

The Vehicle for Injections of Novarsenobenzol

Amongst the causes of accidents due to the use of arsenobenzol, great importance has been attributed to the liquids used in preparing the solutions ; the *question of the water* has been the subject of numerous investigations, and, in the production of toxic accidents. all impurities of the water, both chemical and microbial, have been incriminated ; salts of lead, alkaline silicates, bicarbonate of lime or magnesia, derived from the glass of the distilling apparatus, copper if this was in metal. Chloride of sodium was also blamed if the injection was made with physiological serum. It was not sufficient for the water to be distilled, it was

necessary that it should be distilled at least twice, the last time being on the day itself, or the evening preceding, its use ; further, it was imperative that it should be distilled in an apparatus made of special glass.

When novarsenobenzol was first used it was dissolved in 150 to 200 cubic centimetres of fluid, like arsenobenzol.

Ravaut * made a great advance in the technique of treatment by novarsenobenzol when he showed that the question of water could be solved in a very simple fashion, by reducing the quantity of the vehicle ; by injecting less liquid, and thus injecting a smaller quantity of toxic substances contained in it.

But when a liquid is injected into the veins it must not alter the blood corpuscles and cause hæmolysis.

Traditionally, to avoid hæmolysis, it was customary to dissolve the novarsenobenzol in physiological serum. Ravaut showed that solutions of novarsenobenzol respect the integrity of the blood corpuscles provided a certain content of arsenobenzol is maintained : this content, in his opinion, is 0·45 gr. for 10 cubic centimetres of distilled water. Therefore for the injection of a full dose of novarsenobenzol, 0·45 gr. or more, only 10 cubic centimetres of distilled water need be used, with a proportionate volume for smaller doses, say 3 cubic centimetres for 0·15 gr. of novarsenobenzol.

Later, Ravaut † showed that the quantity of liquid injected could be still further diminished. The solubility of novarsenobenzol in water is such that *two cubic centimetres* of water will dissolve 0·90 gr. These

* Ravaut, "New Process of Intravenous Injection of Neosalvarsan" (*Bulletin de la Société française de Dermatologie*, February 7th, 1913, p. 118). Ravaut and Scheikevitch, "Study on the New Process of Injection of Neosalvarsan in Concentrated Solutions" (*Annales de Dermatologie*, April 1913, p. 208).

† Ravaut, "New Simplification of the Technique of Concentrated Intravenous Injections of Arsenobenzol" (*Presse médicale*, October 1915, p. 398).

concentrated solutions do not alter the blood; they cause no inconvenience, except that they may be painful if, by accident, the fluid is injected outside the vein (see "The Technique of Intravenous Injections," p. 650). It is wise, however, to make the injection more slowly than with larger quantities of solutions.

The water problem is solved by the method of concentrated injections, and to such a point that it is no longer even necessary to use distilled water for these injections. In a hospital at the front, Ravaut has performed injections with water that had been simply boiled and filtered through absorbent wool, without causing any accident.

I have myself proved on several occasions that injections of novarsenobenzol, dissolved in ordinary water, which had been sterilised by boiling for some minutes, do not cause accidents of any kind, and no greater febrile reaction than those made with freshly distilled water.

Nevertheless, one must not use water too highly charged with calcareous salts, as they would react on the novarsenobenzol. When it is impossible to obtain any other, calcareous water may be used, if it is boiled a long time, in order to precipitate the calcareous salts, and then sterilised afresh by boiling after decanting.

To summarise, injections of novarsenobenzol may be made with physiological serum, distilled water which has been prepared less than three months, preserved aseptically or recently boiled, and in case of urgency with ordinary water boiled and filtered through cotton-wool, in a volume *of two cubic centimetres* per injection. whatever the dose of novarsenobenzol.

This method of highly concentrated injections is recommended on account of its simplicity, and the facility with which the necessary material and appropriate syringes can be obtained. It is also recommended because of its innocuousness, by reducing the accidents due to the drug to a minimum. It is the

only method I have used in my hospital work for the past year ; it responds better than any other to the requirements of antisyphilitic therapy in the Army and at the medical centres.

Balzer and Dumouthiers have recommended *intramuscular injections* of novarsenobenzol. This method, which may be compared to injections of insoluble mercurial preparations, has the advantage of not introducing a high dose of arsenic into the circulation ; it is therefore less dangerous than the method of intravenous injections.

Injections, in doses of 0·25 gr., are made twice a week.

As a rule, they are painless, but sometimes painful.

But, as with intramuscular mercurial injections, the possibility of painful local reaction prohibits the adoption of this method for the army. Moreover, its therapeutic action appears to be both less intense and less rapid than that of intravenous injections.

The Effects of Novarsenobenzol on Syphilitic Manifestations

Like arsenobenzol, but in higher doses, novarsenobenzol has a very rapid action on the cicatrisation of *syphilitic chancre*, even in its early stages, and no matter what its extent. From the very first days, the chancre becomes of a paler colour, its borders are less marked, the basal induration diminishes, its appearance resembles that of simple ulceration, its surface contracts, and, within the space of 6 to 12 days, it has completely cicatricised ; the satellite glands, once treatment has begun, cease to increase in size, become less hard, and within a few days again resume their normal dimensions.

The effects are no less remarkable *on secondary lesions*. The *mucous plaques* of the genital organs, anus and mouth are very rapidly influenced by the drug. If they are of the erosive form they heal in

4 to 6 days; hypertrophic plaques, even the most voluminous, subside from the first 2 or 3 days following the first injection, lose their papillomatous appearance, and in 12 to 15 days, *i.e.* after the second injection, they have completely disappeared, without any local treatment.

Cutaneous lesions are also influenced rapidly by novarsenobenzol; as with all active treatment, mercurial, as well as arsenical, they are often the seat of a more or less local congestion, known under the name of Herxheimer's Reaction, during the first hours following the injection. After this temporary congestion, they fade rapidly and disappear; roseola in 5 to 8 days, papular syphilides with large papules in the space of 6 to 8 days, syphilitic plaques of the skin a little more rapidly; papular syphilides with small papules resist treatment more and do not always disappear after the third or even the fourth injection; ulcerous syphilides heal fairly rapidly, and their cicatrisation may be complete in 8 to 15 days, even if they are extensive and deep.

The rapid influence of arsenobenzol on cutaneous lesions of syphilis, especially on ulcerous syphilides, has led some authors to state that the principal effect of this drug is to hasten cicatrisation, and some have denied that it had any other quality.

It is incontestable, however, that it has an action on the visceral manifestations of syphilis, which is as rapid as that which it exercises on the cutaneous lesions.

Secondary syphilitic *headache* is nearly always influenced by it. It is not unusual for patients suffering from violent headache and consequent insomnia for several days to regain sleep the night or following night, after the first injection. The same thing applies to the pains in the limbs, which are sometimes so distressing in secondary syphilis.

More serious troubles, such as hemiplegia of the

face and limbs and medullary lesions of secondary syphilis, are also influenced rapidly.

Iritis and Irido-choroiditis are very quickly modified by novarsenobenzol ; the preorbital pain yields in a few days, sometimes in a few hours, the iris regaining its contractility and coloration ; no more adhesions are produced, and in fifteen to twenty days the iris has resumed its normal aspect, with the exception of a slight sluggishness and some tendency to dilatation, and, of course, the cicatrised remains of adhesions prior to treatment.

The *general condition* of the patient responds very rapidly to the influence of arsenical medication ; the febrile condition common in secondary syphilis subsides in two or three days, the sensation of fatigue so frequent in the early stages, the pallor or earthy colour of the face, rapidly give place to a sensation of well-being, normal coloration of the skin, and renewed vigour. Many syphilitics declare that their health is far better since treatment with arsenobenzol than it was before the onset of syphilis : they soon put on flesh to a noticeable extent, their appetite returns, and often the growth of hair is more abundant than it was before. The above are the effects of any active arsenical medication, at the maximum of intensity and rapidity, owing to the richness of the drug in arsenic.

With patients who had previously been subjected to mercurial medication and in whom this drug had reacted on the buccal mucous membrane, a very rapid modification of the mercurial gingivitis must be added to these favourable effects : the ulcerations become clean and heal, salivation ceases and mercurial treatment can be renewed later on without bringing about a return of the stomatitis.

To sum up, in the great majority of cases, excepting the rare instances of intolerance or resistance to the drug, novarsenobenzol, like arsenobenzol, rapidly causes the disappearance of the lesions of primary and secon-

dary syphilis, and at the same time improves the general condition of the patient to a degree not attained by mercury.

This is undoubted, and evidence would have to be repudiated if it were not acknowledged.

The question is, whether the action of arsenobenzol is symptomatic—a rapid and energetic action on the lesions only, or fundamental—a curative action on the disease itself. In a word, does novarsenobenzol "whitewash" the syphilitics, or does it cure syphilis?

I have already said that the *sterilisatio magna* announced by Ehrlich has not been realised by a small number of injections of arsenobenzol. Can this result be obtained by multiplying the injections, and using higher doses of the drug?

Opinions vary. Some hold that sufficiently energetic treatment will cure syphilis radically and definitely. According to others, this result is never attained.

One fact seems now to be established, *i.e.* that, in order to hope to sterilise syphilis by arsenobenzol or by novarsenobenzol, the disease must be attacked from the primary period, preferably from the second or third weeks of the chancre, and that, once the secondary troubles have appeared, one can no longer expect such a result.

In what proportions has this sterilisation been realised in cases of syphilis treated from the onset? This is difficult to ascertain. Some authors claim results which are truly marvellous. But their statistics are generally based on the experience of a few months, and their statement that syphilis has been sterilised rests on the fact that no symptoms have been seen during the period of observation, and that the Wassermann rection became and remained negative.

This last argument is inadequate, no matter what has been said, to justify one in asserting that the syphilis has been cured. Prolonged observation during several years would alone authorise this conclusion.

In fact, syphilis, treated either by mercury or not at all, may remain for many years without any external signs, and yet manifest more or less serious symptoms at the end of 12, 15 years and more—I have even seen a case after 54 years.

An apparently more weighty argument has been supplied by the fairly numerous observations of several medical men, who, after treating a syphilitic chancre by arsenobenzol, have seen a new one develop later. In virtue of the axiom that an infective disease which recurs is one in which the first attack has been cured, one must conclude that the first attack of syphilis had been cured.

I have already shown, with regard to the diagnosis of syphilitic chancre (see page 566) the probable explanation of some lesions—the majority, in my opinion—regarded as reinfection chancres in patients treated by arsenobenzol.

Apart from the pseudo-chancre of reinfection, later syphilitic manifestations are often seen in patients treated by arsenobenzol.

After a latent period of several months, lesions of the mucous membranes, simple or hypertrophic plaques, may appear, often accompanied by a circinate erythematous eruption, of the type of recurrent roseola (see p. 574) which respond again to treatment with arsenobenzol or mercury, sometimes to again reappear after a variable period.

Other syphilitic manifestations of different kinds and varied locations may also appear, especially nervous affections, and these I shall mention again.

What is remarkable is that the most characteristic symptoms of the secondary period are usually absent; the typical roseola is not observed in patients treated with arsenobenzol. Again, delayed lesions of the tertiary type often occur at a period at which they would not have had time to appear in untreated syphilis or that treated by mercury. Arsenical medication

seems both to retard or inhibit the appearance of early lesions and hasten the appearance of the later manifestations of syphilis.

Detractors of arsenical medication have taken advantage of the appearance of these delayed lesions, and have cited cases in which they appeared after arsenical treatment of varying intensity and duration.

It is impossible to deny that patients treated by high and repeated doses of arsenobenzol, from the first days of the chancre, have presented indubitable syphilitic lesions, of a more or less serious character, at the end of a few months.

On the other hand, trustworthy observers have cited cases treated from the first days of chancre with arsenobenzol, in which the Wassermann Reaction has become negative and remained so for two or three years, without the appearance of any syphilitic trouble.

It is, therefore, justifiable to conclude that arsenobenzol may definitely cure syphilis, when it is employed at the initial period,* but also that definite cures obtained with this drug are rare, no matter at what period of syphilis it is instituted or what dose is given.

With regard to the Army, this conclusion should lead medical men to regulate the use of arsenical medication in the hope of attenuating syphilis, and curing it if possible. It does not justify them, however, in endeavouring to obtain a result which is always exceptional, by means of extremely energetic and prolonged medication which would prevent the patient from performing his military duties and diminish the number of efficient soldiers.

This consideration is of importance, owing to the fact that it is not certain whether very high doses and prolonged use of arsenobenzol may not have a noxious effect. During the six years in which arseno-

* See specially Brocq's *mémoire* ("How to administer Salvarsan," *Annales de dermatologie*, December 1912, p. 669) in which this question is handled with the greatest caution.

benzol has been used, we cannot pretend to be acquainted yet with its remote effects. When the nervous system frequently responds to arsenobenzol by a reaction which ends in grave disorders, it is possible that too energetic initial treatment may lead to more or less pronounced inflammatory conditions, and perhaps predispose to terminal localisations of the treponema in the grey matter.

There is a risk, of which the civil surgeon should warn his patient, when proposing an energetic abortive treatment, but which the army surgeon does not appear to have the right of imposing upon the men who are confided to his care.

In what Doses should Novarsenobenzol be injected?

The most varied and contradictory opinions have been stated as to the suitable doses of the arsenical compound to be injected.

Ehrlich, relying on his experimental researches, fixed the dose of arsenobenzol at one centigramme per kilogramme of body weight, and stated that this should never be exceeded at one injection. Assuming that the toxicity of novarsenobenzol is two-thirds that of arsenobenzol, the maximum dose for a man of average weight of the new compound is 1·5 centigramme per kilogramme.

The great majority of authors agree that it is never necessary to give this dose, and no one advises it for the first injection.

All agree that the first injections—or at least the first one—should be made with smaller doses than the succeeding ones. By a massive dose at the beginning, too great a number of the treponemas are destroyed at one stroke, and the products of bacteriolysis add their noxious action to those of the drug, and cause intense reactions. Further, as experience has proved, the organism has to become accustomed to the toxicity

of the arsenic, so that a dose, which at the first injection would cause toxic troubles, does not do so if the ground has already been prepared by previous injections. This tolerance disappears, or is at least attenuated by time, so that if medication by arsenobenzol or novarsenobenzol is resumed after a period of rest, the first injection must be made with a smaller dose than the last of the preceding series.

Finally, it seems evident that the susceptibility of all patients to the toxicity of arsenobenzol is not the same ; the first injection enables one to feel one's way, and reduce the dose of this drug in subjects who are intolerant.

For all these reasons, it is rational, and experience has shown it necessary, not to give the highest dose of the drug at the beginning of treatment.

But with what dose should one commence ? Some authors, alarmed by the accidents observed, have proposed that one should start with very small doses, 0·30 gr., or even 0·15 gr. of novarsenobenzol, and increase this progressively by 0·15 gr. at each injection.

Others, not less expert in therapeutic matters, commence with 0·60 gr. of novarsenobenzol, reach 0·75 gr. at the second injection, and often keep to this dose for the following ones ; they do not seem to have had more accidents with this method than others who are more cautious.

Every one has been guided in his line of conduct by the facts observed and the theories he has evolved.

As far as I myself am concerned, I was struck by two fatal cases in young women after small doses of novarsenobenzol. In one case, the first injection had been made with a dose of 0·20 gr., the second of 0 15 gr. ; in the other case, the injections were respectively 0·30 gr. and 0·45 gr. As I constantly use larger doses without accident, I do not consider that weak initial doses are free from risk, and think there is no danger in commencing with a dose of 0 45 gr. in healthy

men. In women I generally reduce the initial dose to 0·30 gr., and even in men who are anæmic, or nervous subjects upset by the idea of the danger of arsenobenzol, or presenting some taint or suspected history (albuminuria, cardiac disturbance, etc.).

With young and healthy subjects, like most men serving in the Army, the initial dose of 0·45 gr. never shows any contra-indication. By beginning with an active dose, one has the advantage of reducing the duration of treatment and hospitalisation, an advantage which, in time of war, must always be aimed at, if it is not purchased too dearly.

When the first injection has been badly borne and has caused a febrile reaction, arsenic intolerance must be suspected. It is, therefore, prudent to suspend the use of the drug, at any rate for a time, and, if imperative to again resort to it, the weakest doses must be given, 0·15 gr. for example, and its effects carefully watched.

In the following injections, the dose should be increased to 0·60 gr. and 0·75 gr. In the majority of cases, contagious lesions are cicatrised after the second injection, given in a dose of 0·60 gr., and if necessary we can limit ourselves to these, on condition, as I shall show later on, that mercurial treatment is continued. Many of my patients, who were given two injections only, before being subjected to mercurial treatment, did not later present any syphilitic symptoms.

Nevertheless, I consider that it is more efficacious to begin with a dose of 0·45 gr., which is fairly high ; the therapeutic effect of two successive doses of 0·45 gr. and 0·60 gr. is at least equal to that of these two doses preceded by one injection of 0·15 gr. or of 0·30 gr.

If the cure of the contagious troubles is delayed, a fresh injection will generally have the desired effect.

Some authors consider that a cure is more certain and durable, and the chances of the return of syphilitic

symptoms more remote, if the treatment is continued. They also advise that the injections should be continued until a total dose of about 3 grammes has been reached, which represents an injection of 0·45 gr. and four injections of 0·60 gr. or one injection of 0·45 gr., one of 0·60 gr., one of 0·75 gr., and one of 0·90 gr.

The utility of such doses is not evident to me ; I do not think that they have an absolutely prophylactic action against later troubles, and I consider that this action is obtained more certainly by the association of mercury.

Periodicity of the Injections

It is necessary to have intervals between the injections, in order to permit the organism to eliminate the drug, which requires four to five days, and to recover from the shock induced, and the humoral and visceral troubles that have been provoked. It is admitted almost unanimously that the interval between two injections should be a week. Even if small doses of the drug are injected, it is not wise to have them closer together.

The After-effects of Concentrated Injections of Novarsenobenzol

As Ravaut has shown, the after-effects of concentrated injections of novarsenobenzol are generally very slight.

If the patient's temperature is taken carefully every three hours, it will frequently be found that a rise begins six to eight hours after the injection. This rise of temperature, which is quite as high after dilute injections, is more intense after the first injection than after subsequent ones ; it is specially marked in patients suffering from secondary symptoms, who have been recently subjected to mercurial or arsenical treatment. It is generally absent after subsequent injections.

The temperature may rise to 40° C., but as a rule does not exceed 38°, and falls at the end of 6 to 8 hours.

This early febrile reaction, due to the effect of the drug on the treponema, must be distinguished from a delayed reaction, occurring the day after, or two days after, the injection, which rarely exceeds 39·5°, does not last beyond twenty-four hours, and seems due to toxic phenomena.

With certain patients, the injection of novarsenobenzol is followed by a slight fall of temperature, below 37°, some hours after the injection. This is much more frequent after the third and following injections than after the first.

In many patients the rise of temperature is not accompanied by any noticeable malaise. In others there is headache, usually mild. This headache is of little importance unless it increases with subsequent injections of larger doses.

Also, nausea and vomiting are not exceptional after the first injection, which they follow almost immediately, but are rare after subsequent ones.

Some patients suffer from diarrhœa on the night following the injection, but this is rarely severe, although sometimes sanguinolent.

The following are the after-effects of injections observed in my clinic, where the injections are always made in concentrated solutions.

The injections are made between 10 a.m. and noon, the patient resting quietly afterwards and only taking a small quantity of liquid. The temperature taken in the axilla every 3 hours from 3 p.m. did not exceed 37·5°. *i.e.* a figure which may be regarded as normal in 80% of the cases ; in 32% it remained below 37°. With certain patients it rose to 37·2° or 37·3° at 3 p.m., reaching its maximum at 6 p.m., then falling to 37° at 9 p.m., and remaining at that figure during the night. With other patients it reached its maximum at 3 p.m. ; then fell to 37° at 9 p.m. and remained

below 37° during the night or at 6 p.m. These patients experienced no trouble or discomfort of any kind.

In 18% of the cases the temperature rose above 37·5° but did not exceed 38·5°; this rise was generally of short duration, and reached its maximum at 3 p.m. or 6 p.m.; the patients often had no malaise, but some had a slight rigor, passing headache, or some nausea. These febrile attacks were observed especially in patients who had intense secondary cutaneous manifestations. In one patient I saw a generalised scarlatiniform eruption; in another an urticarial eruption a few minutes after the injection.

In 2% of the cases there was marked rise of temperature, reaching 40° C. at the same time that the patients suffered from rigors, headache, and nausea, which were more intense than in the preceding cases, but only of short duration.

Such are the reactions, which may be called normal, after concentrated injections of novarsenobenzol: they have no real importance, and the fear of them should not prevent recourse to the drug. The attenuating influence that previous mercurial treatment has on them should make one precede the injections of novarsenobenzol by mercurial treatment whenever possible. I shall again revert to this point.

Other accidents may, however, result from this medication. They are similar to those observed with other methods of treatment by arsenobenzol or novarsenobenzol. These are the accidents which have so frightened certain medical men, and compromised the arsenical treatment of syphilis. They are much more rare with concentrated injections than with other methods. All the same, they must be described here.

The Serious Accidents of Arsenobenzol and Novarsenobenzol

It is impossible to separate the accidents caused by novarsenobenzol from those produced by arseno-

benzol; although much less frequent with novarsenobenzol, they are of the same order and may be of equal gravity.

The conditions of development of these accidents are multiple, their pathogeny is complex, and still a matter of dispute. Their interpretation has given rise to discussions, sometimes acrimonious, into the details of which I cannot enter without exceeding the limits of this book. I shall content myself with giving a brief summary of the most important of them.

It must be remarked, first of all, that certain of these accidents cannot be attributed to the drug, but to ignorance of its contra-indications. It would be impossible to-day to include, amongst accidents of the medication, the serious consequences which may result from its use, especially in high doses, in subjects suffering from grave lesions of the heart, liver, kidneys, and in cachectic patients. In these pathological conditions, the administration of arsenic is contra-indicated.

Again, the method cannot be blamed for the fatal results of injections made with arsenobenzol, the composition of which has changed from contact with the atmosphere, or with solutions prepared in advance, the toxicity of which results from chemical transformations of the arsenobenzol.

The reduction of the amount of liquid injected has eliminated the noxious action of the water and of its chemical impurities; the substitution of novarsenobenzol for arsenobenzol has done away with the accidents produced by the insufficiency of alkalinisation of the solutions of the original product.

The uncertainties of dosage which always occur on the first appearance of any new drug have long ceased; the excessive doses preferred by some authors have been the cause of accidents, which no longer happen with those in use at the present time.

The number of serious accidents, and especially of

deaths, tends to diminish more and more, and is infinitely less, especially with the method of concentrated injections, than during the first years in which arsenobenzol was employed.

The serious accidents caused by arsenobenzol and novarsenobenzol specially affect the *nervous system*.

The gravest of these accidents takes the form of *acute encephalitis ;* it appears sometimes after the first injection, more often after the second, and rarely after the subsequent ones ; it generally begins in the three first days following the injection, rarely later.

It is characterised by severe headache, rise of temperature, facial congestion, delirium, followed by coma, repeated epileptiform attacks, and vomiting, generally leading to death within a few hours.

At the post-mortem, intense hyperæmia of most of the organs is found, and particularly punctiform hæmorrhages in the cerebral substance ; at the same time lesions of acute nephritis are often present.

The great majority of deaths following the administration of arsenobenzol, and more rarely novarsenobenzol, belong to this type. It occurs not only in patients suffering from visceral troubles, but also sometimes in healthy, young, and vigorous subjects, in whom there was absolutely no warning of what was about to happen, and this after moderate doses of the drug. It must be recognised, however, that inexplicable deaths from arsenobenzol have become the exception.

Encephalitis appears more frequently after the second injection of arsenobenzol than after the first. Its development must be specially suspected in subjects who, after the first injection, presented an intense febrile reaction, facial congestion, the phenomena described by Milian under the name of nitritoid crises, and especially morbilliform or scarlatiniform cutaneous eruptions.

It is advisable with patients who have suffered from

reactions of this kind, after the first injection, to suspend treatment, or at least only to employ moderate doses.

Besides this grave form, there is a series of phenomena, of a less tragic character, described under the name of *neuro-relapses*. These consist chiefly in paralysis of the cranial nerves.

They appear some weeks after treatment is finished, and are preceded, during some days or weeks, by headache of varying intensity, diffuse or predominating on the side of which the paralysis is situated, and pains in the nape of the neck, the back, or limbs. According to the statistics of Bénario, this paralysis affects the auditory nerve in 44·5% of the cases, the optic nerve in 30·2% ,the oculomotor nerve in 7·4% and the facial nerve in 7%.

Affection of the auditory nerve is manifested by tinnitus, auditory hallucinations, unilateral or bilateral deafness, which may be accompanied or not by slight vertigo and rarely by vomiting.

Lesions of the optic nerve result in optic neuritis, neuro-retinitis or retinitis with stasis of the pupil, often without very pronounced functional troubles.

Lesions of the oculomotor and facial nerves give rise to paralysis of the corresponding muscles.

The unilateral or bilateral lesions sometimes affect several cranial nerves simultaneously; hence the variety of clinical syndromes, sometimes rendered more complex by the co-existence of lesions of the spinal nerves: paralysis of the type of Landry's disease, polyneuritis, intercostal neuralgia, etc.

Lumbar puncture reveals abundant lymphocytosis of the cerebro-spinal fluid.

Functional disorders generally recover after a variable period; but auditory affections may persist indefinitely.

These different lesions result from compression of the cranial nerves by basilar meningitis, often associated

with latent spinal meningitis, which is only revealed by lumbar puncture.

These facts have been the subject of various interpretations. When arsenobenzol was first used, their frequency caused them to be attributed solely to the toxic action of the drug. It was soon remarked, however, that lesions of the same kind were observed in syphilitics before the use of arsenobenzol, only less frequently ; and, on the other hand, that they were only observed amongst syphilitics and never appeared in patients treated with arsenobenzol for affections independent of syphilis. Attributed to the neurotrophic action of arsenobenzol, they were soon put down to the action of the pathogenic agent of syphilis, hence the name of neuro-relapses, which has been given them. This denomination is disputable because it is not a question of the recurrence of previously existing lesions, but it has entered into current language. It is recognised to-day almost unanimously that, if the lesions are of a syphilitic nature, arsenobenzol may favour their development.

As Ravaut has shown, syphilis frequently causes meningeal lesions, which remain latent clinically, and are only revealed by changes in the cerebro-spinal fluid (lymphocytosis, albumin), which are exacerbated by arsenobenzol, resulting in neuro-recurrent phenomena. The *neurotropism* of arsenobenzol, which has been invoked to explain the production of these accidents, does not exist, according to Ravaut, unless the nervous system is already invaded by the treponema. This explains why these lesions are observed especially in syphilitics treated too late with arsenobenzol, at a period when the treponema has already reached the nervous system, and do not occur in patients submitted to arsenical injections from the very onset of the chancre.

The frequency of these lesions is diminished by associating mercury with arsenobenzol, especially

when the arsenobenzol treatment is preceded by a course of mercury.

The various organs may present more or less acute reactions under the influence of arsenobenzol.

Icterus is sometimes observed; it appears to be favoured by renal insufficiency. It often accompanies fatal encephalitis, but may also exist alone. It is presented under very variable aspects, from a rapidly curable form to a fatal one, with symptoms of grave icterus (acute cirrhosis, yellow atrophy of the liver). The pathogenesis of the icterus of arsenobenzol has not been definitely elucidated.

Albuminuria appears in some cases to be provoked by arsenobenzol. It often happens that long-standing albuminuria may be exaggerated or reappear; it may persist and be accompanied by uræmic troubles; it ceases if arsenical treatment is at once interrupted.

Gastro-intestinal disorders which are usually hardly noticeable, sometimes attain a certain intensity: repeated vomiting, copious diarrhœa.

Cardiac disturbance rarely becomes pronounced, except in the case of a lesion of the heart, and especially of aortic aneurism, which forms a contra-indication to the use of the drug. It is usually limited to palpitations, or at most lipothymia, which forms part of the nitritoid crises.

Cutaneous eruptions of an erythematous, rubeoliform, or more frequently scarlatiniform type may occur after injections of arsenobenzol, usually about the second day; they constitute a sign of severe intoxication. Some cases of generalised exfoliative erythrodermia have occurred from the use of arsenobenzol.

To sum up, multiple, grave, even fatal lesions may follow injections of arsenobenzol and of novarsenobenzol. The pathogenesis of some of these seems to be established; in the case of nervous lesions, the phenomena are comparable to Herxheimer's Reaction,

and are probably due to the action of the arsenical products on tissues already inhabited or altered by the spirochæte. In others, the pathogenesis remains obscure.

One fact has been established, namely, that these disturbances are less frequent and not so grave with novarsenobenzol as they are with arsenobenzol, and that concentrated injections still further reduce their number and gravity.

It is none the less true that they may exceptionally follow injections made quite correctly, and without there being anything to indicate their approach.

Fear of these disturbances must, nevertheless, not prevent recourse to arsenical medication, especially in the case of young patients; for indeed this sometimes protects the patient from syphilitic manifestations, which are often graver and in any case more frequent.

Other Arsenical Preparations

Various other products with an arsenical basis have been proposed for the treatment of syphilis.

I may recall the fact that, before Ehrlich's discovery, benzo-sulpho-para-aminophenylarsinate of sodium, sold under the name of hectine, had a certain vogue; its activity being much lower than that of arsenobenzol and novarsenobenzol, preference has been given to these two last substances. It has no special indication in army medicine and cannot replace novarsenobenzol. The same applies to its combination with mercury, under the name of hectargyre.

Mouneyrat discovered another arsenical compound, tetraoxydiphosphaminodiarsenobenzene, described by the number 1116, which is sold under the name of galyl. This substance is presented in the form of a yellow powder, without either smell or taste, insoluble in water and the majority of neutral solvents. When placed in a weak solution of carbonate of soda, it

dissolves instantly and yields a brown or yellowish brown fluid. According to its promoters, galyl is less toxic than arsenobenzol, causes no congestive phenomena, and is tolerated well. They say, it should be used for man in a total dose of 1·50 gr. spread over three injections with an interval of eight days between each.

Whatever its activity or innocuousness, this product, like the original arsenobenzol, Ehrlich's " 606," has the inconvenience of not dissolving, except in an alkaline medium. If the dosage of carbonate of soda is not absolutely accurate, and this seems to offer some difficulty, either an imperfect solution is obtained or a hyperalkaline fluid, which irritates the walls of the veins and causes painful indurations, independently of any operative unskilfulness. For this reason, this drug does not seem to me to be suitable for army medicine.

More recently, Danysz proposed a complex arsenical compound for the treatment of syphilis, containing antimony and silver, stibico-argentic sulphate of dioxy-diaminoarsenobenzol, described by the number 102, and placed on the market under the name of luargol.

The compound is presented in the form of a yellowish-orange powder, which, like other products of the arsenobenzol series, has to be preserved in hermetically sealed vacuum tubes. It is insoluble in water, but soluble in dilute alkaline fluids, forming a very dark brown solution, which changes rapidly in a bright light, and more slowly in the dark. *This solution must be filtered before use.* Its toxicity appears to be lower than that of arsenobenzol, and its greater activity enables one to obtain therapeutic effects comparable to those of novarsenobenzol, with smaller doses. Owing to its weak toxicity, it seems to me to be very useful in the treatment of syphilis in exhausted, overworked, and elderly patients.

Luargol has the inconveniences of all substances

which only dissolve in an alkaline medium; even in the hands of experts, it sometimes produces venous changes, distension of the vein at the moment of injection, with subsequent pain and induration of the vein; it cannot, therefore, be recommended as a suitable drug for the Army at present.

To sum up, the different agents of arsenical medication, in experienced hands, may give satisfactory results in the treatment of syphilis. Those who have had much experience with one of these substances may prefer it to the others. In army practice, where it is necessary to treat patients actively, rapidly, and with the least possible risk of local and general disturbances, in my opinion, with the limited material at our disposal in the medical centres, one can only recommend novarsenobenzol for the routine administration of arsenical treatment.

Association of Mercury and Arsenic

When intensive arsenical medication was first commenced, Ehrlich announced that syphilis was sterilised by arsenobenzol; one might have believed that mercury was going to be removed from the list of antisyphilitic drugs.

To-day, even, some medical men believe that arsenobenzol suffices for the treatment of syphilis from its onset to its latest periods. Their number has never been very large, and I believe that it is diminishing more and more.

As a matter of fact, all medical men, even those who have retained the greatest belief in arsenobenzol, have seen patients thus treated—not only with novarsenobenzol, which may be less active, but also Ehrlich's salvarsan—with high doses and repeated injections, who have, nevertheless, shown grave syphilitic manifestations, often a short time after the last injections. Patients, having first received 3 to 5 grammes of

arsenobenzol in 6 to 8 injections, then one or two series of similar injections, who had had no lesion beyond a chancre, have come to consult me for roseola of the type of recurrent roseola, or for a papulo-tubercular syphilide. I repeat, every one has seen similar facts, the reproduction of which has become significant.

No doubt syphilitics have shown grave syphilitic disturbances directly after mercurial treatment, even during its course, and after it had been followed carefully for what was regarded as an adequate period.

But, having regard to the relative number of patients treated intensively with arsenobenzol, the cases are much more frequent in which this drug has not prevented later disturbances.

Hence, the majority of syphilologists are of opinion that it is at least advantageous—most say a necessity—to complete the arsenical treatment of syphilis by a course of mercury.

By means of this combined method the patient benefits, on the one hand, by the quickness of action of the arsenobenzol, the rapid healing of lesions, and, in cases of primary or secondary syphilis, by its markedly retarding action of secondary manifestations; on the other hand, by the greater security offered by mercurial treatment as a prophylactic measure against later manifestations.

The association of mercury and arsenobenzol has another advantage, upon which Ravaut has rightly insisted. If administered before the arsenical treatment, mercury kills a certain number of treponemas; the first injection of arsenobenzol will therefore destroy a smaller quantity of treponemas, and consequently the proportion of bacteriolytic products distributed in the circulation will be sensibly diminished. The result is that the fever, the intensity of which is directly due to intoxication by the bacteriolytic products of the treponema, is less in patients first treated by large

doses of mercury.* This result is particularly important to obtain in the secondary period, with cutaneous and mucous manifestations which are rich in treponemas.

For these reasons there is almost complete unanimity amongst syphilologists as to the necessity of combining mercurial and arsenobenzol treatment.

But how are these two drugs to be combined? Must they be prescribed simultaneously, alternatively or successively? Here, as for the dosage of the drugs, all kinds of opinions are expressed; each syphilologist has his own method, derived from his theoretical conceptions of the effects of the drugs and from the good or bad results he has witnessed.

Some authors are afraid of using mercury at the same time as giving arsenical treatment, and dreading accidents, especially with secondary syphilitics, do not begin arsenobenzol until after a prolonged mercurial treatment, stopping the mercury directly they commence using arsenobenzol.

The majority of syphilologists consider that these fears are exaggerated, and that the two drugs may be alternated and combined without danger.

For my own part, I have interposed injections of cyanide of mercury between injections of arsenobenzol in hundreds of cases, and have not seen any bad effects. I have, therefore, no scruple in preferring this method of treatment.

In military practice it has the advantage over the successive or alternative use of the two drugs of reducing the duration of treatment, the intervals between the injections of arsenobenzol being made use of for the mercurial treatment, or at least for a considerable part of this treatment. During the primary and secondary periods, when contagious lesions compel the patient to be sent to hospital, it is then possible, without loss of time, to combine the arsenical treatment simul-

* Ravaut and Scheikevitch, *loc. cit.*

taneously with the most active mercurial treatment. In this way, the whole weight of the attack is at once brought to bear upon the syphilitic infection from its onset.

SCHEME FOR THE TREATMENT OF SYPHILIS IN THE ARMY AT THE DIFFERENT PERIODS OF INFECTION

After describing the different methods of treatment of syphilis, their advantages, disadvantages, and dangers, it is necessary to consider the course to be followed in the treatment of syphilis in the Army.

Here, again, it is only a question of formulating routine *treatment* of syphilis, which the medical man must modify, according to the particular conditions of the patients and of their disease. With regard to military patients collectively, relatively few differences are found in general conditions of age, health, physical resistance, etc. Syphilitic manifestations being generally observed in them at an early stage and under fairly similar forms, this routine treatment will have more chance of responding to the indications of the great majority of cases than it would in the case of any other group of patients.

I again repeat, that the treatment must be instituted in such a way that it will *reduce to a minimum* the ineffectiveness of the soldier. In order to do this, every soldier suffering from contagious syphilitic lesions —sent to hospital on account of contagion and necessarily isolated—should, while in hospital, be subjected to *energetic treatment* capable at the same time of causing rapid cicatrisation of the contagious lesions and of combating the general infection, and preventing, or at any rate attenuating, subsequent manifestations treatment *by attack and barrage* against syphilis.

Further, when the syphilitic patient has left hospital, he should continue treatment when with his unit, in

order to prevent relapses of the disease at a more or less distant date : *continued* treatment, prevention of later disturbances.

I shall only describe the treatment of syphilis at the chancral period and at the secondary period; tertiary disturbances and the sequelæ of syphilis play only a small part in war syphilology.

Period of the Chancre.—Once the diagnosis of chancre has been undoubtedly established, the syphilitic should be subjected to injections of novarsenobenzol *with as little delay as possible*, and sent to hospital for that, as well as to put him out of the way of doing any harm.

It is useful, but not absolutely indispensable, to precede the arsenical treatment by two or three intravenous injections of mercury : I say useful, because I have often seen the chancre partly cicatrise under the influence of these injections alone, and also because a febrile reaction is sometimes produced after the injection of arsenobenzol, and this reaction is attenuated by the initial injections of mercury.

After these injections, one of novarsenobenzol in a dose of 45 centigrammes is given ; eight days later, an injection of 60 centigrammes of novarsenobenzol. *If imperative*, arsenical treatment can be left at that.

Nevertheless, when the chancre has not completely cicatrised 4 or 5 days after the second injection of arsenobenzol, or if the initial dimensions of the chancre were considerable, or accompanied by pronounced adenopathy, or had not been treated until after 15 to 20 days, it is necessary to make a third injection 8 days after the second, of 0·60 gr. of novarsenobenzol. In any case, if military duties do not prevent it, it is advisable to make this third injection.

In the intervals between the novarsenobenzol injections, an *intravenous injection of cyanide of mercury* (1 centigramme) is given daily or every other day ; 12 to 15 injections in all.

As it is preferable not to make the cyanide injection on the day following the injection of arsenobenzol, treatment lasts altogether 18 to 24 days.

On condition that it is followed by regular treatment by mercurial pills, in the way that will be described later on, this is sufficient, *in the great majority of cases*, to protect the man from secondary disturbances : I had practised this method some time before the war with a certain number of syphilitics, and have been able to observe the results.

In any case, if syphilitic manifestations appear later, they are hardly likely to be of any considerable intensity.

As regards tertiary affections, I cannot affirm that they need no longer be feared, but is there any other method of treatment by arsenobenzol in larger and oftener repeated doses that is a certain protection ?

I must mention that, before subjecting the patient to injections of cyanide of mercury, his teeth must be examined, and attended to, if necessary.

At the same time as this internal treatment, it is almost unnecessary to prescribe local treatment of the chancre : washing in boiled water, dressings of wool dipped in boiling water, or, if desired, applications of powder of sub-nitrate of bismuth are sufficient to guarantee its cleanliness and prevent infection. Calomel powder or calomel ointment should not be used, as they cause irritation. Touching or painting with nitrate of silver should also be avoided; it is useless and does not visibly hasten the cure of chancres treated by arsenobenzol, and, in a general way, the use of antiseptics should be dispensed with.

In chancres of the urethra local treatment also consists in washing with boiled water. I do not advise that any dressings should be introduced into the canal ; the patient should drink large quantities of fluid to dilute the urine and render it less irritating.

Chancres of the lips should be dressed with boiled

water, or covered with a piece of thin and clean paper (cigarette paper, for instance); the lips should be washed with boiled water after each meal.

In *chancres of the tonsils* the throat should be irrigated with physiological serum; emollient, carbolic, or iodine gargles may be used.

The Secondary Period.—Not only in cases with active secondary symptoms, but also in those where the chancre is present, but has been untreated, general treatment is almost identical with that of the period of the chancre.

Here, for the reason already indicated—attenuation of the febrile reaction induced by arsenobenzol—it is highly important to precede the novarsenobenzol injections by two, three (even four if cutaneous eruptions and mucous plaques are abundant) *intravenous injections of cyanide of mercury.* Then at weekly intervals, two or more, often three *injections of novarsenobenzol* are made in the doses already recommended (0·45, 0·60, and 0·60), with interpolated injections of cyanide of mercury, so that 15 to 20 centigrammes of cyanide are given during the period of treatment, which lasts from 18 to 25 days.

Once this treatment is over, the patient must continue treatment in his unit with pills of protoiodide of mercury.

While under treatment in hospital, secondary ulcerous manifestations are attended to by *local treatment*: washing of the mucous plaques in the genital region with Labarraque's solution (solution of hypochlorite of sodium) in the proportion of two to three tablespoons per litre of water; cauterisation of the hypertrophic plaques every two days with acid nitrate of mercury,* or, failing that, touching with a nitrate of

* Acid nitrate of mercury is, without doubt, the most active and efficacious caustic for ulcerous lesions of secondary syphilis, especially for hypertrophic plaques. It must be handled with care, otherwise large and deep eschars may be caused. The following technique will guard against any accident: dip a piece of cotton-

silver pencil; touching the buccal mucous plaques with nitrate of silver or with a 50% solution of methylene blue, slight touches of acid nitrate of mercury on the hypertrophic plaques of the lips, tongue, etc.

In *severe ulcerous lesions of the skin* (malignant syphilides), which are very rare, however, in military practice, arsenical treatment must be pushed still further both as regards dosage and duration, and must be continued after the ulcerations are all healed. One should make 5 to 6 injections of arsenobenzol in doses of 0·45, 0·60, 0·60, 0·75, 0·90. At the same time, syrup of iodide of iron should be prescribed, together with a nourishing diet and fresh air.

Certain forms of cutaneous lesions of the secondary period often resist arsenical medication, even if intensive; *papulous syphilides with small papules* (follicular, miliary, lichenoid, and acneiform syphilides). It is necessary in these forms to repeat the injections of novarsenobenzol and combine them with intravenous injections of cyanide of mercury. It is sometimes an advantage to make one or two injections of calomel, and, when the resources of the medical centre permit this, to let the patient have some sulphur baths. But, as these lesions are of slow evolution, neither ulcerated nor contagious, the man is not prevented from performing his military duties, and I do not think it advisable to prolong his stay in hospital. If, at his depot, he can obtain the necessary attention, is doing sedentary work, or is engaged in munition works, from which he can attend, once a week, for an injection of novarsenobenzol, he can be discharged from hospital at the end of 15 to 20 days.

wool rolled tightly around a wooden stick into the solution of acid nitrate, press the stick against the side of the bottle to express any superfluous fluid, gently touch the affected surface with the stick, and, *as soon as it becomes bleached*, pass a thick plug of wadding full of pure water over the surface. Contact with the water will at once stop the pain caused by the acid nitrate, so that cauterisation is much less painful with it than it is with nitrate of silver.

In the case of a syphilitic with secondary lesions who has already been treated with arsenobenzol, there need be no hesitation in continuing the same drug under the form indicated above, and even in pushing the doses still further, providing that this treatment has not caused symptoms of intolerance.

Some visceral manifestations demand special medication, even contra-indicating the above treatment.

Syphilitic headache at the beginning of the disease, with nocturnal predominance, does not often appear to be very severe amongst soldiers, apart from those who exaggerate it in the hope of escaping either from treatment or from their military duties.

Treatment, according to the foregoing rules, generally causes it to disappear rapidly; very frequently it yields after the first injection of arsenobenzol. Should it persist and prevent sleep, iodide of potassium may be given (1 to 2 grammes daily) or a mild hypnotic (opium).

Should the headache be really intense and persistent, it may be well to make a lumbar puncture, the value of which would be twofold. In the first place, it often relieves the headache; secondly, examination of the cerebro-spinal fluid enables one to find out the condition of the nervous centres; if there is abundant lymphocytosis present, more prolonged treatment should be instituted, especially with arsenobenzol.

Facial paralysis, appearing in the secondary period, with or without previous arsenical treatment, in itself reveals affection of the nervous system, and requires energetic treatment. I consider it is wiser, when it appears during the course of arsenical treatment, to keep to mercury, in the form of intravenous injections of the cyanide, or intramuscular injections of calomel. Treatment should be prolonged till the disappearance of the headache which often accompanies it, and until the paralytic symptoms have become attenuated.

Later, the patient should be kept under prolonged medical supervision and treatment.

Early *syphilitic hemiplegia* also demands energetic treatment, similar to that I have just described for facial paralysis. Although it may be completely cured, without sequelæ, it may lead to temporary or permanent disablement.

The same applies to early *meningitis*.

Iritis is much more frequent than paralysis, and also necessitates active treatment, both arsenical and mercurial. There should be no hesitation in giving 4, 5, or even 6 injections of novarsenobenzol, until a total dose of 2·50 gr. to 3·25 gr. has been reached, and at the same time large doses of mercury should be administered and continued during the arsenical cure. Local treatment should also be instituted, and consists in the use of atropine, alternating or not with that of eserine. In a case where the patient cannot be rapidly subjected to examination by an ophthalmic surgeon, in order to prevent the formation of iritic adhesions, 4 to 5 drops of the following eye-lotion should be used daily by instillation :

Neutral sulphate of atropine	0·10 gr.
Distilled water	10 gr.

Icterus of the secondary period of syphilis should be treated with mercury : intravenous injections of cyanide are nearly always tolerated well, but all the same their effects must be watched carefully, on account of intestinal hæmorrhage. In default of these injections, recourse may be had to intramuscular injections of soluble salts, and the internal use of calomel in small doses. Opinions differ as to treatment with arsenical compounds. Owing to the eclective toxicity of arsenic for the liver, I consider that it is better not to have recourse to it during the presence of icterus, nor till the liver has regained its normal volume. Also the diet must be attended to very carefully.

Syphilitic nephritis, manifested by hæmaturia and albuminuria, which is often considerable, requires great care in the administration of active anti-syphilitic drugs.

If it is evident that the albuminuria is due to syphilis, and is not of long standing and due to pathological conditions prior to syphilitic infection, anti-syphilitic drugs are indicated; but, as these medicaments are more or less toxic for the kidney, and may add their action to that of the syphilitic virus to form a chronic and incurable lesion, rapid but not too intensive action is required.

Intravenous injections are followed by rapid elimination of mercury by the kidneys; it is dangerous, therefore, to give too high doses, especially at the beginning of treatment. In such cases, it is my custom to give the injections every day in small doses, beginning with 0·0025 gr. increased gradually to 0·005 gr. and 0·0075, and, if the albuminuria does not increase, up to a centigramme at the end of eight to ten days. The albuminuria has then generally decreased slightly and the use of novarsenobenzol may be commenced; but only in small doses, 0·15 gr. or 0·30 gr. at the maximum. While carefully watching the urine, the doses of novarsenobenzol are raised to 0·30 gr., 0·45 gr., 0·60 gr., the last being repeated until a total of 2·50 gr. to 3 gr. has been reached.

At the same time, the patient is kept in bed until the albuminuria has disappeared, and put on milk diet.

Lesions of the muscles and bones rarely attain any very considerable degree in secondary syphilis, and only exceptionally necessitate any special treatment. Nevertheless, osteitis causes osteocopic pains which may prevent sleep. Mercurial, and especially arsenical, treatment acts very effectively on these pains. Sometimes however, it is preferable to administer iodide of potassium (1 to 3 grammes daily) at the same

time as mercury. Local applications, especially mercurial plasters, combine the resolvent action resulting from their composition and the slight absorption of mercury with an analgesic action of occlusion. Sometimes it may be necessary to have recourse to hypnotics: opiates, bromide, and even chloral, at least during the early days of treatment, and until this has acted on the lesions.

Continued Treatment.—The preceding treatment is destined to combat active syphilitic manifestations, to hasten the disappearance of contagious lesions, and check syphilitic infection so as to attenuate later manifestations. It is insufficient to prevent the return of syphilis, or its hereditary influence.

It is necessary, therefore, that it should be followed by complementary treatment, and prolonged during several years.

On leaving hospital, the syphilitic must be informed that it is imperative for him to continue treatment during an adequate period. To be realised practically, this continued treatment must be simple, and not interfere with the performance of his duties.

In the Army several conditions have to be considered.

At the Front there is only one method of treatment which is suitable, the use of pills, tabloids, or cachets of protoiodide of mercury, in the dose of 10 centigrammes of protoiodide daily, in 4 pills. The periods of treatment, as a general rule, will be regulated in the way to be described later.

Should any contagious disturbance appear, the patient will be again sent to a venereal centre.

Should a non-contagious manifestation appear, which does not prevent military service, the patient should take a larger dose of protoiodide (five to six pills daily) and during a longer period, while on duty.

Sometimes, however, when the regiment is resting and in the proximity of a venereal centre, or is provided with a competent medical man, the patient may be

given one or two injections of arsenobenzol, or some soluble mercurial injections.

In the *depots* and *sedentary services* preparations of protoiodide are also the most suitable for continued treatment ; but it is more feasible to make use of injection. Whenever indicated, injections of arsenobenzol may be made ; these only necessitate a day, or half a day's, absence from duty. If the doctor is accustomed to making intravenous injections, it will be easy to arrange it. As to intramuscular injections, soluble or insoluble, these should be reserved for men whose duty will not be interfered with by a slight and temporary pain on walking.

For munition workers, whose mode of life differs but little from that of workmen in times of peace, treatment is easier to carry out.

Whenever possible, it is advantageous to make two or three injections of novarsenobenzol in doses of 60 centigrammes, at intervals of eight days, about two months after the initial treatment in hospital. Each of these injections only necessitates rest for a day or half a day, and could be made either at the end of the day or at the time of the half-weekly rest.

Mercurial treatment can be carried out by means of pills, as with the soldiers at the front ; but, in any case, it is preferable to give injections, either intravenous of cyanide, or intramuscular of soluble preparations, when the medical service allows patients to submit, without loss of time, to an injection every second day, or to injections of grey oil when it is only possible to give them once a week.

Continued mercurial treatment, no matter what preparations are used for it, should be carried out, as far as possible, on the following lines, from the point of view of periodicity and duration : First, 20 days per month during the 3 months following hospital treatment.

For the next 9 months, 12 to 15 days per month.

and during the following year 12 to 15 days every two months.

Later on, mercurial treatment should be repeated during 2 or 3 years, twice a year for 40 to 50 days.

It must be again emphasised that, during the course of this treatment, the patient must take care of his teeth, and brush them every day; that treatment must be suspended if troubles attributable to the mercury occur—salivation, stomatitis, diarrhœa—to be again resumed later with precautions; that, if syphilitic symptoms appear, mercurial treatment must be reinforced or completed by injections of arsenobenzol according to the nature and gravity of the disturbances; in a word, it must be adapted to the indications presented.

It may be remarked that, in the regulation of this treatment, I give no place to the indications furnished by *the Wassermann Reaction*. Besides being difficult to carry out regularly with all the patients during the course of their disease, I consider, with many authors, that this reaction is of *no value* from the point of view of indication and regulation of treatment. It is an excellent diagnostic method within the limits where its accuracy can be relied on; but, whatever one may say, it does not furnish a single precise fact as to the possibility of the return of syphilitic disturbances. It may be negative in patients who, a few days previously, presented severe symptoms; again, it may be positive at a given moment, and then become negative without the patient having received any treatment.

Having regard, on the one hand, to this uncertainty, and, on the other hand, to the well known preventive action of mercury employed in the form of successive treatments during the first years of infection, patients should be given the benefit of repeated intermittent mercurial treatment without paying any attention to the results of the serum-reaction.

CHAPTER VI

TECHNIQUE OF INTRAVENOUS INJECTIONS

As we have seen in the preceding chapter, intravenous injections play an important part in the modern treatment of syphilis. Although they do not constitute a method reserved exclusively for syphilis, and are to-day largely used in therapeutics, it seems necessary that I should here give details of the technique. The following description will, I believe, enable any medical man, who will follow it regularly, to perform the injections without any great difficulty.

Nothing is so good, however, for perfecting the technique of injections as frequenting a hospital where they are performed constantly.

Instruments

The apparatus required for intravenous injection is very simple. All the essentials are found in every medical centre, and, being constantly used for the most varied diseases, they are always kept in stock.

It includes :

(1) *An all-glass syringe*, with a capacity of 1 or 2 cubic centimetres, for injection of cyanide of mercury, and 2 cubic centimetres for concentrated injections of novarsenobenzol. In case of urgency, one might use a syringe of 1 cubic centimetre for the latter, when 30 centigrammes of arsenobenzol are injected, and fill it twice for higher doses. Syringes holding 5, 10, and 20 cubic centimetres may also be used for injecting

2 cubic centimetres of the solution, but they necessitate the use of an intermediary nozzle, which may get lost, and, owing to the size of the piston, this requires a greater effort of pressure ; it is therefore, preferable to use a syringe with a small capacity.

(2) *The needle.* Any needle that pierces well and is not too large is good, on condition that the operator knows how to use it.

The bevel of the needle should be as slight as possible, so as to avoid an accident, to which I shall refer

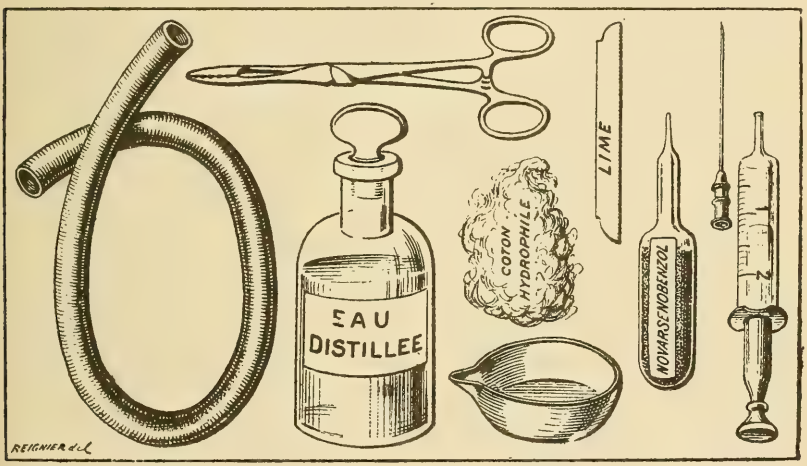

FIG. 1.—Apparatus required for the Intravenous Injection of Novarsenobenzol.

later on ; but it must not be too flat-nosed, because needles of this kind pierce badly.

I much prefer needles of *steel* to those of either platinum or nickel, as they pierce better ; if they are well taken care of, *i.e.* are kept greased, they do not become oxidised and last for a long time ; further, they can be easily sharpened, and are not expensive. There is no advantage in a platinum needle, especially as for intravenous injections it has always to be sterilised in an autoclave or in boiling water ; if sterilised in a flame, there is always danger of the

formation of carbon concretions in the bore of the needle.

Some medical men have suggested various devices, such as the use of a rubber attachment to the syringe. Clement Simon * has devised a bent attachment to the syringe, in order to facilitate the introduction of the needle into the vein, and allow of its being directed almost parallel to the skin. When it is only necessary to inject a small quantity of fluid (1 or 2 cubic centigrammes), these arrangements have the inconvenience of making the amount of drug injected uncertain. They have no practical advantage; they are easy to lose, and difficult to replace.

(3) A *rubber tube* for a tourniquet.

(4) If the medical man works alone, or with a somewhat inexperienced assistant, he must have a pair of pressure forceps to fix the tourniquet.

(5) *Absorbent wool.*

(6) An *antiseptic fluid* for disinfecting the skin. I advise the use of alcohol or ether for asepsis before making the injection, because they are colourless, and do not cover up the vein, and tincture of iodine for aseptic purposes after the injection.

(7) The *product to be injected.*

Also, if novarsenobenzol is to be injected:

(8) *Distilled or boiled water* for making the solution †; and

(9) A *small receptacle* (porcelain or glass) for making the solution, although the ampoule containing the drug may be sufficient.

* Clement Simon, "Technique of Intravenous Injections" (*Journal de Médecine et de Chirurgie pratiques*, June 10th, 1918).

† As novarsenobenzol is completely soluble in water, it is not necessary to filter the solution, and the expensive and fragile apparatus provided for filtration is useless if care is taken not to aspirate the very last drops of the solution into the syringe.

When boiled water is used, one must be certain of its filtration without risking contamination. Ravaut has proposed a very simple device for this purpose. This consists in applying the extremity of the syringe against the wall of the receptacle in which

The syringe, needle, and receptacle intended for preparing the novarsenobenzol solution must of course be sterilised, either in a steriliser or by prolonged boiling in pure water. In places where the water is very chalky, in order to avoid precipitation of carbonate of lime in the needle, syringe, or receptacle, sterilisation must be effected either by distilled water, or water which has already been boiled, and decanted.

Mode of Operation

The liquid to be injected having been prepared and aspirated into the syringe; this, armed with the needle, is placed on a table close to the operator; it rests on a sterilised compress, or simply on the edge of the table in such a way as to avoid contact with any non-sterilised object. The table should by preference be to the right of the operator.

He places the patient opposite to him, seated on a chair, or sits down beside the bed in the exceptional cases in which the patient cannot get up. The patient's arm, bare to the middle of the biceps, rests either on the knee of the operator, on the edge of the table, or, more preferably, is held by the operator's left hand. The rubber tourniquet is applied at the junction of the middle and lower third of the patient's arm, stretching it before encircling the arm. If the operator is alone, he clips the band by means of pressure forceps, taking care not to catch up the skin. If he has an assistant, the latter holds the tourniquet

the water has been boiled, interposing a tampon of wool, which has also been boiled, and aspirating slowly; the wadding acts as a filter, which the fluid is compelled to pass through in order to penetrate into the syringe.

A glass tube, open at the end, can also be immersed in the receptacle while the water is boiling; for example, the body of a large-sized syringe, at the bottom of which a tampon of wool has been carefully placed: the water passes through the wool filter before flowing perfectly clear into the upper part of the tube, or it can be aspirated with the needle.

tight until the needle has been inserted into the vein.

At the same time, if the veins are not very prominent, the patient is told to close the fist or flex and extend the fingers, so as to make the veins swell. The operator, or his assistant, rubs alcohol or ether over the bend of the elbow.

The next step is to select the vein into which the injection is to be made; all veins at the bend of the elbow, of the lower part of the arm, and upper part of the forearm, may be utilised. With the majority

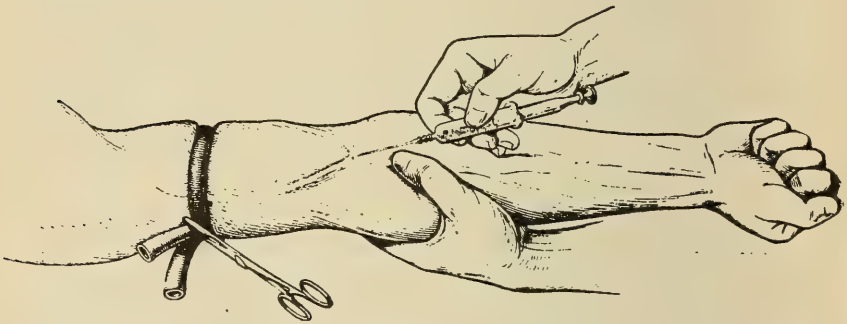

FIG. 2.—*First stage of the injection.*—Position of fingers of the right hand holding the syringe. Position of left thumb holding the vein. The syringe is directed in the axis of the vein and almost parallel to the surface of the limbs.

of vigorous men, all veins are equally apparent and may be used with equal propriety; with patients who have already had injections, there may be venous indurations, which limit the extent of utilisable vessels. The operator chooses preferably not from amongst the most visible and most distended veins, but from those which are most swollen and most perceptible to the touch. In patients whose veins are but slightly apparent, or in whom the development of subcutaneous adipose tissue is similar to that of a woman, the veins can be felt by palpation.

The operator then takes the syringe armed with the needle in his right hand, holding it between the thumb

and fingers, the little finger being left free to act as a support on the patient's arm. He traces the vein with the index finger of the left hand ; then, having clearly determined its position and direction, grasps the patient's arm with the left hand in the following manner : the palm and four last fingers are applied to the posterior surface, while the thumb, placed on the anterior surface, draws down the skin along the selected vein, so as to fix it and prevent its slipping from under the needle (see Fig. 2, page 656).

The needle is held with its bevel turned up at an

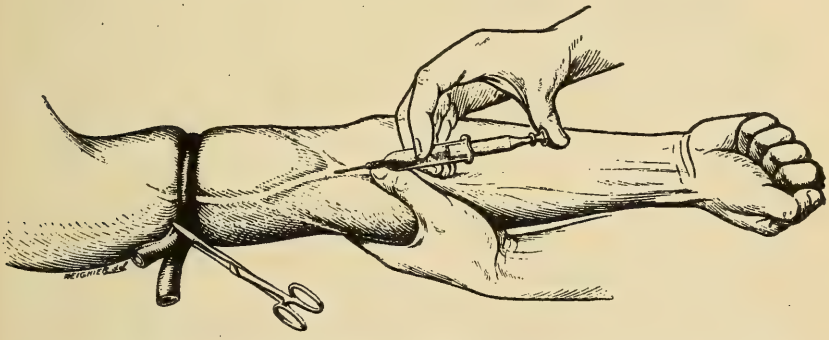

FIG. 3.—The needle has been inserted into the vein, while being held parallel to the skin. Blood has flowed into the body of the syringe. New position of the fingers of right hand : the thumb holds the extremity of the syringe before injecting the solution. The left thumb has not been moved.

acute angle almost parallel to the surface of the limb. The operator introduces it in the direction of the vein, puncturing the skin, then pressing forward almost immediately to penetrate the vein ; in this second movement it is necessary to further reduce the angle of the needle with the skin and direct the needle almost parallel with it (see Fig. 3).

The penetration of the needle into the vein is signalled at the same time by a feeling of void at its extremity, and by the penetration of blood into the body of the syringe. Sometimes, however, blood does not at once flow into the syringe, although one is convinced

that the syringe is in the vein ; it is only necessary to make slight traction on the piston with the left hand to see blood flow into the syringe.

If the needle has not penetrated the vein at the first attempt, it should be withdrawn gently and a fresh attempt made to introduce it. In the case of failure, make a fresh puncture of the skin at a different place, where the position of the vein appears more favourable. Care must be taken, however, in the event of the puncture of the skin having drawn blood, to make the fresh attempt on the other arm.

It sometimes happens that the needle is blocked by a small clot of blood, which prevents the blood from flowing into the syringe ; therefore, before attempting to make a fresh injection, it is well to convince oneself of the permeability of the needle, by pressing the piston.

When the operator is certain that the needle has penetrated the vein, the rubber tourniquet is loosened. He now has only to push the contents of the syringe into the vein ; for that he exercises continuous pressure on the piston, either by means of the right thumb, the syringe being held in position between the index and second and third fingers, the little finger still serving as a support (see Fig. 4, page 659), or by means of the left hand.

At this stage it is necessary to be certain that the fluid is flowing into the vein, and has not been introduced either into its wall or into the perivenous cellular tissue. The penetration of fluid into the tissues causes immediate pain, both with cyanide of mercury and novarsenobenzol ; directly the patient experiences any pain other than the very slight one of piercing the skin—which moreover is caused at the beginning and not during the course of the injection itself—the operation must be stopped at once, an attempt made to place the needle more correctly, or, better still, recommence the injection at another place.

Another indication of this escape of fluid is the production of œdema at the seat of puncture. The operator must keep his eye on the operative zone during the whole course of the injection : at the slightest swelling of this region he must suspend all pressure of the piston.

Any abnormal resistance of the piston to the thumb must give rise to fear that the fluid has passed into the venous wall. When this is felt the piston must be gently withdrawn ; if the needle is in a good position, blood flows into the syringe ; if it does not, the needle must be immediately withdrawn.

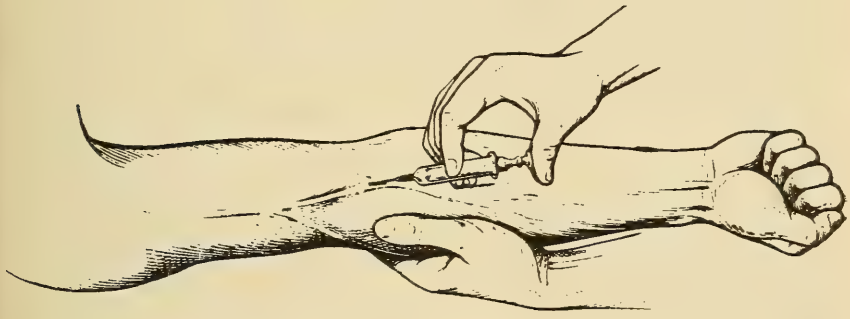

FIG. 4.—The tourniquet has been removed. The right thumb pushes the injection into the vein. The left hand supports the forearm.

If a little air has got into the syringe, it is best to stop the injection before the piston has got to the end of its course, although the introduction of air into the veins is not so dangerous as was formerly supposed.

Once the injection has been made, it is well to draw back the piston and withdraw a few drops of blood, to relieve the extremity of the needle from the caustic fluid which, by drying on the venous wall or in the cellular tissue, might cause an inflammatory reaction.

It only remains to withdraw the needle and put a tampon of wool soaked in alcohol, or, better, in tincture of iodine, on the puncture.

After the injection is finished the patient may go

back to his work, except after injections of novarsenobenzol, when he must rest for a while.

If a few drops of blood issue from the little wound, this hæmorrhage can be easily overcome by putting a tampon of wool on the puncture and telling the patient to flex his elbow strongly for some minutes.

After the injection, the syringe must always be carefully washed in cold water, and the needle must be syringed through several times to prevent any blood remaining and coagulating. If a steel needle is used, it must be dried by air, injected with vaseline and greased with the latter.

Intravenous injection, despite the minute technicalities I have just described, is nearly always a simple and easy operation which can be performed by any careful and fairly skilful surgeon. After a few days' practice it can be made very rapidly, in fact, quite as quickly as a simple subcutaneous injection. In my hospital clinic, with one assistant compressing the arm, and another cleaning the syringes and needles, and having them boiled, my pupils succeed in making sixty injections in an hour, including the time necessary for charging the syringes. I have even seen pupils make as many as thirty injections, without accident, in a quarter of an hour. It is, therefore, not difficult in a venereological section on active service to treat the majority of patients by this process, on condition that the assistants are intelligent, careful, and well trained.

It must be recognised, however, that with certain subjects an intravenous injection presents certain difficulties. This is rarely the case with vigorous adult men, with whom alone we have to deal here. Sometimes, however, the veins at the bend of the elbow are small, buried in adipose subcutaneous tissue, and difficult to find, even on palpation. If none can be felt in this region, the injection must be made in the forearm where it is rare not to find a sufficiently

large vein on the outer side ; the position the patient is obliged to assume to present it to the operator is uncomfortable for both, but the injection is possible. It is only as a last resource that an injection should be made in a vein of the lower limbs, because, owing to the frequency of varicose veins, infection is easier and more serious than in the upper limbs.

One difficulty may arise, not from the smallness, but from the mobility of the veins, which sometimes causes inconvenience to beginners : the vein slips away and cannot be perforated by the needle. To prevent this, the best method consists in holding the vein in position by means of the left thumb, in the way I have recommended above. It has also been proposed that, instead of piercing the vein in its prominent part, it should be approached laterally, by introducing the needle into the skin a little outside the vessel, and then pushing it slowly towards the vein ; the limit of its elasticity is soon reached, it ceases to escape from the point, and can be perforated by the needle ; when penetrated, the vein becomes distended and resumes its normal position.

Operative Accidents

The only operative accidents which may result from an intravenous injection are the introduction of the injected fluid into the venous wall, and its penetration into the perivenous cellular tissue.

Intraparietal penetration may occur when the orifice of the needle is too elongated. It may happen that the orifice is partly in the internal tunica of the vein and partly communicates with the lumen ; when the operator aspirates the syringe, blood flows into it, and the operator consequently believes that he is in the lumen of the vein, but the remainder of the orifice of the needle draws the injection fluid into the vascular wall itself. This causes immediate pain,

followed by an inflammatory reaction with painful induration which persists for several weeks, and may hinder the continuation of treatment.

The penetration of the fluid into the perivenous cellular tissue may occur either from the side or front of the vein, or behind, when the needle has been introduced roughly or at too wide an angle, and has passed through the vein from one side to the other. This penetration, as I have already stated, may be avoided or arrested at once, if care is taken to watch closely the injection zone, and the patient is advised to at once report any unusual pain. With cyanide of mercury and novarsenobenzol, which are very irritating substances, there is acute pain, the production of a more or less extensive inflammatory nodule, and often an eschar which may attain the dimension of a shilling, become detached slowly, leave a loss of substance, and ultimately an adherent cicatrix.

When this accident is observed, the intensity of inflammation and subsequent dimensions of the eschar may be notably reduced by immediately performing massage of the region, so as to cause reflux of the greatest possible quantity of noxious fluid by the track of the needle. Further, compresses soaked in fresh water should be applied at once and renewed frequently.

It is not rare, even after an injection which has been properly performed, for a subcutaneous ecchymosis to appear, due to infiltration of blood from the passage of the needle into the cellular tissue : this is an incident of no importance.

Some patients complain of acute pain the moment the skin is pierced, which persists for some minutes extending down the forearm. This occurs when a nerve filament has been injured by the needle, but this pain never lasts long.

Finally, with the exception of eschars, which may be avoided almost entirely, given careful technique,

there are never any accidents of importance caused as the result of intravenous injections. I do not know of a single case of subsequent embolism, even if venous indurations have developed.

Precautions to be taken after Intravenous Injections of Cyanide of Mercury

Mercury, injected into the veins in the form of cyanide, is absorbed very rapidly, much more so than with any other form of mercurialisation. This is one of the advantages of the method, but it may result in the possibility of an accident, which must be recognised and warned against—mercurial colitis.

Certain subjects, the majority having previously suffered from digestive disorders, some hours, or perhaps even within an hour, of the intravenous injection of cyanide of mercury, are suddenly seized with acute pain in the region of the colon, violent rectal tenesmus, more or less copious diarrhœa, with first sanguinolent, than hæmorrhagic stools. These symptoms may last one, two, or three days, and, owing to the loss of blood, cause pronounced anæmia. Treatment consists in the internal use of opium in adequate doses, the administration of emollient enemas, and application on the abdomen of wool soaked in laudanum or large linseed poultices with laudanum.

These accidents may be prevented almost certainly if, at the time of injection, the patient is given an opium pill of two or five centigrammes, as I have made a rule of doing in my hospital clinic.

It may be mentioned that these accidents are produced almost exclusively after the first or second injection of cyanide. With subjects who seem predisposed to intestinal troubles and with elderly or exhausted patients, I have, therefore, made it a rule to give the first injection of cyanide in a dose of half

a centigramme, or even of a quarter, and increase this gradually.

When the patient has had an attack of colitis after the first injection of cyanide, treatment may be resumed with this method later, after waiting a few days and recommencing with small doses of cyanide.

Injections of cyanide of mercury must also be used with circumspection in the case of albuminuric patients. Some patients have a recrudescence of their albuminuria after the injections, resulting from the irritative action of mercury on the kidneys. Treatment must not be continued with these patients. With others, no disturbing effects at all are noticed, but both urine and diet must be under constant supervision.

As with all mercurial treatment, the teeth and gums must be examined before giving cyanide of mercury injections, and kept under observation during treatment. However, owing to the rapid elimination of the drug, stomatitis is rare in patients treated by this method.

All the same, if only by way of precaution and to accustom the patients to take the necessary care of their mouth and teeth during mercurial treatment, they must be ordered to wash out the mouth twice daily with white soap or with a tooth-powder containing a sufficient proportion of soap.

Precautions to be taken after Intravenous Injections of Novarsenobenzol

As I have shown above, the after-effects of arsenobenzol injections are generally mild. Especially with the method of concentrated injections, these are nearly always reduced, when they do occur, to transient rise of temperature, of which the patient has sometimes no knowledge.

But, in order to obtain this result, it is necessary that the patient should have only had light food, not

less than three hours before the injection, and that, afterwards, he should keep quiet and be dieted.

For hospital patients, rest in bed immediately after the injection, and for the whole day, is the rule.

When patients only come into hospital for the injection, they can return home at once on foot, if they live near, otherwise drive, and go to bed for the day. They can resume their ordinary work the following day.

During the day following the injection, they must be kept on a strict diet; water and liquids are alone permitted; at most they may be allowed some soup or an egg five hours at least after the injection.

I have seen patients seized with rigors, intense fever, profuse sweating, and repeated vomiting, after having disobeyed these orders and taken even a light meal.

CHAPTER VII

HYGIENE OF SYPHILITIC SOLDIERS

HYGIENIC measures, although often neglected, are of the utmost importance in syphilis.

A considerable number of these measures are superfluous, or impracticable, in the case of soldiers. There is no need, in the Army, to recommend rest, fresh air, moderate exercise and no late hours, such as are prescribed for civilians.

Useful advice, which can be put into practice when the men are in camp or at the base, is to keep the body clean, especially the genital organs, by means of washing, baths, or douches; these are precautions all soldiers should take whenever they have the opportunity.

The following advice is specially suitable for syphilitics.

(1) *Suppression of Tobacco.*—This should be proscribed for all syphilitics, at any rate during the first year of the disease. Tobacco, no matter under what form, pipe, cigarette, cigar, or quid, is the principal exciting cause of buccal mucous plaques. A syphilitic, who is well treated, and neither smokes nor chews, is almost certain to escape them. In hospital, the doctor must insist upon total abstinence from tobacco for all syphilitics.

When the man has returned to his unit he often ignores this prescription; it is the duty of the medical man to remind him of it. When a patient has had

numerous recurrences of buccal mucous plaques, and continues to smoke despite repeated orders to the contrary, he should be threatened with military punishment.

(2) *Hygiene of the Mouth.*—After the use of mercury, stomatitis often develops in patients whose buccal mucous membrane is not in good condition, especially in the region of the gums and teeth. It is indispensable that all syphilitics should take particular care of the mouth.

The patient's teeth must be examined before treatment is commenced, and, if necessary, they must be cleaned by a dentist, and all bad teeth stopped. During mercurial treatment this examination should be repeated.

Further, every day during mercurial treatment, the teeth and gums should be cleansed twice or even thrice with a brush, soap and water, or with a powder containing soap.

Salol, frequently recommended for cleansing the mouth, has an irritant action on the skin, and often causes eczema of the labial commissures ; any preparations containing it should be severely avoided.

Many medical men prescribe mouth washes of chlorate of potash for their syphilitic patients. This solution has merely a detergent action and has no advantage over simple boiled water. As a prophylactic measure against mercurial stomatitis, it is far inferior to a soap-wash. Hence, I see no reason for recommending it.

(3) *Drinks.*—Syphilitics must avoid the abuse of alcohol, take wine moderately, and refrain from all liqueurs and spirits.

(4) *Clothing.*—Mercury easily induces diarrhœa; syphilitic patients should, therefore, avoid getting cold in the abdomen, and a flannel cummerbund is recommended.

(5) *Sexual Relations.*—Syphilitics should refrain from

sexual intercourse during the first months, even where no contagious lesion is to be found on the genital organs. As a matter of fact, the blood is contagious at this period, and there is always risk of an excoriation being produced during the sexual act.

The patient must be advised as to the dangers of contagion, of the lengthy period during which it may exercise its influence, and of the necessity for consulting a medical man before marriage, or, in the case of married men, of resuming marital relations.

CHAPTER VIII

PROPHYLAXIS

The prophylaxis of syphilis concerns not only the military, but also the civil population, more than any other contagious disease which may attack the Army, owing to its conditions of transmission. It constitutes a social danger, against which every competent and authorised effort should be directed, for it can only be combated by measures carried out by the combined action of the military and civil authorities.

These measures, of unequal importance and variable scope, should be carried out with vigilance, energy, and perseverance if satisfactory results are to be obtained. They concern men who are infected with syphilis, men who are not infected, and women who may contract and transmit the disease. They may be classified in two main groups :

1. Measures intended to prevent infected men from transmitting syphilis ;

2. Measures intended to prevent healthy men from contracting syphilis.

NECESSARY PRECAUTIONS FOR PREVENTING THE TRANSMISSION OF SYPHILIS BY INFECTED MEN

These measures are all within the province of the military authorities ; they are given in simple rules or circulars emanating from headquarters, and can be easily applied.

The majority of these measures were already in

force in peace time; the increased frequency of syphilis as the result of the war renders their execution much more urgent: the circulars of the Under-Secretary of State of the Army Medical Service, dated January 5th and September 25th, 1916, set these out officially.

The carrying out of these measures really depends less on the officer in command than upon the doctor, whose duty it is to see that they are performed in each particular case.

Isolation of Syphilitic Carriers of Contagious Lesions

Syphilis is transmitted exclusively by direct contact of the secretion product from one of the lesions. Thus, it can only be transmitted by *open* syphilitic lesions, and then only during the early stages; later ulcerative lesions are only exceptionally contagious.*

On the other hand, these open lesions become cicatrised, either spontaneously, or under the influence of treatment in a relatively short time. As regards treatment, I have shown that the cicatrisation of a chancre, or of mucous plaques, subjected to energetic medication at once is a question of fifteen to twenty days at the utmost.

Therefore, to prevent a syphilitic patient from doing any harm, it is necessary, and in all probability sufficient, to isolate him during fifteen to twenty days, both in the case of infective chancre, and mucous plaques of the genital organs, anus, mouth, or pharynx.

As a rule, these symptoms attract the attention of the patient sufficiently to induce him to consult the doctor.

All the same, it is imperative that all syphilitic patients should be examined by the medical officers of their company: many pay little attention to a

* Transmission by blood does exist, but it is so rare that it need not be taken into account in prophylactic practice.

small, painless sore, causing no inconvenience, of which they suspect neither the nature nor danger, especially if it be a dwarf chancre or single mucous plaque. Some are afraid of being sent to hospital, or deprived of leave, if they complain of a lesion of the genital organs, while others, again, dread treatment or fear to divulge their malady.

In short, despite the recommendations and good intentions of the medical officers, many syphilitics escape examination and remain in the regiments, unless the doctors have permission to search for them and succeed in running them to earth.

Medical Inspection

Even in times of peace, regimental orders provide for the *medical inspection* of the men, especially as regards venereal disease, at the time of enlisting, and when going on leave and returning.

These visits include examination of the genital organs, anus, and buccal cavity. In order to be really efficacious in the discovery of the great majority, if not of the total number, of syphilitics, the medical man must bring to bear on the case careful attention, and genuine knowledge of syphilitic disturbances of the skin and mucous membranes.

Two conditions are demanded, which are not always forthcoming :

(1) Sufficient time for the examination of each man, which is not possible in many circumstances, especially at the departure for, and return from, leave.

(2) Proper lighting arrangements and instruments necessary for the effective examination of the patients. These requirements are far from being satisfactorily fulfilled in a hut or tent where the light is often bad. As to instruments, these are nearly always rudimentary, and the doctor has to make the most strenuous efforts to see the different parts of the buccal cavity.

It is hardly necessary to mention that all men should be compelled to attend the visit of inspection. Control by the commanding officer and supervision by the non-commissioned officers are indispensable, when certain men who, knowing they are syphilitic, try all they can to evade detection.

The order which, in time of peace, releases non-commissioned officers from medical inspection, does not hold good during war, and should be abolished. It is necessary owing to the conditions of common life in camp, the fact of N.C.O.'s being often younger than their men, and especially on account of the great frequency of syphilis.

It seems difficult, but should be legitimate nevertheless, to compel officers to submit to medical inspection : it is due to medical men attached to the Army to use their influence with officers, and persuade them to consult them on the slightest suspicious manifestation.

The ministerial circular of April 7th, 1912, advises monthly medical visits of inspection. This periodicity is inadequate. The circular issued on September 25th, 1916, was right in advising that they should be made twice a month. To be really efficacious the visit should be a surprise one.

Regulations order the medical inspection of all men starting on leave and forbid that any soldier carrying contagious symptoms should be allowed to go, and another inspection when the men return from furlough. I doubt whether this second order, which is quite rational, is often put into practice.

The visits are made in the *companies of the regiment*, the depots, and the majority of the services in a more or less regular manner, and too much pressure cannot be brought to bear on the doctors as to their importance. In any case, it is imperative that they should also be made in munition works and on all *mobilised workmen*, whether French or belonging to Colonial contingents,

who are working there. These men are under military control, but have more opportunities and facilities than soldiers at the front for contracting and disseminating syphilis, and do not neglect them; moreover, they are very often infected, and in a higher proportion than occurs in soldiers at the front. They should, therefore, be compelled to submit to medical inspection, which should be as rigorous as that of the latter. It would be easy for some arrangement to be made between the medical men and managers of munition works, in order that the inspection could be made at an hour when it would not interfere with work.

Similarly, in the *medical centres* inspection should be made of men who, while under treatment, are given leave to go out, even if only for a few hours. In small localities, as in large towns, a great number of them contract syphilis. The majority, whose manifestations are very evident, cannot dissimulate their condition to the doctor in charge, who takes the necessary precautions; but a certain number of them escape medical control and treatment. Very justly, the circular of September 25th, 1916, prescribes that all wounded under treatment at the different centres should be subjected to bi-monthly inspection, and, in case of venereal infection, treated whenever possible like the men in the depots. I have reason to believe that this inspection is often neglected; it would be invaluable in places where the wounded are kept long, but have frequent leave, particularly in physio-therapeutic, mechano-therapeutic, and neurological centres.

Syphilitics and Hospital Treatment

Every syphilitic patient, who is a recognised carrier of one or more contagious manifestations, should be sent to hospital, at any rate until these symptoms disappear. This is the absolute rule laid down in the circular of

September 25th, 1916, which orders that any patients suffering from chancre or the slightest suspicious erosion must be sent to a venereal hospital. No exception can be allowed, at any rate as concerns soldiers and non-commissioned officers, no matter what their position or employment.

The same rule should be established for officers, but it might be difficult to get it accepted : it is due to the medical officer to decide in each particular case what is best to be done, having regard to the usefulness of the officer in his position, and the precautions he is able to take against disseminating the disease. If hospital treatment is necessary, the medical officer should assert his authority, in order to get this effected ; otherwise, he must carry out energetic treatment himself.

The hospital should be made an absolute rule for all men mobilised in munition works, because they are the most dangerous to the civil population in which they live. Some doctors, in charge of the medical inspection of munition works, when consulted by a workman with chancre, give him a fortnight's rest, so that he may be treated. This practice is deplorable. In the majority of cases, the workman waits some days before going to a hospital, receives a prescription, which is often inadequate, uses it badly, and when the fortnight is over, during which he has rarely failed to contaminate some woman, his chancre has not healed. Every time a mobilised workman has consulted me I have refused to give him a prescription and ambulatory treatment, and have sent him to the doctor of his works with a note indicating the necessity for his being sent to hospital, and I must acknowledge that he has always sent the patient back to me with this object.

Similarly when, from physio-therapeutical or neurological centres, a wounded soldier under treatment has been sent to me with a syphilitic chancre or mucous

plaque, the medical man in charge arranges to send him to me every day, if necessary, for an injection.

Sending a patient to hospital implies really that he will get *active syphilitic treatment* in order to reduce internment to a minimum. I have insisted upon this sufficiently when describing the treatment of syphilis and need not revert to it. The mere fact of being in hospital, in the majority of cases, allows energetic anti-syphilitic therapy. The Under-Secretary of State has insisted upon this very rightly since January 5th, 1916.

In the case of contagious syphilis, the patient, when in hospital, must be isolated; that is to say, during his whole sojourn he must not be allowed to go out, on any pretext whatever. That is evident. In exceptional cases, permission may be given to patients to go out, if their time in hospital has been prolonged by more or less grave general symptoms, or intercurrent diseases; but only on the strict condition that there are no longer any active contagious lesions.*

On leaving hospital, there is no reason for sending syphilitic patients on furlough, as is usually the case with wounded and sick soldiers evacuated from the Front. There is no medical reason why they should not at once go back to duty; their general condition is seldom changed by the disease, and even intensive arsenical medication improves nutrition so much that syphilitics are often in a better condition of health when leaving hospital than they were on admission.

On the other hand also, the concession of leave when discharged from hospital would constitute a sort of premium on the reproduction of syphilitic symptoms, and, if syphilitics are not to be punished

* As refusal of leave is not intended as a disciplinary measure, the remnants of the old-fashioned ideas with regard to "secret" or "shameful" diseases, but merely as a hygienic precaution, it is not well to refuse permission to syphilitics suffering from tertiary lesions, whether ulcerous or not, as there need be no fear of their spreading contagion.

for having contracted the disease, it would be a pity for them to obtain a benefit from it, in the form of leave.

There is justice, therefore, in the circulars of January 5th and September 25th, 1916, having ordained that, on principle, neither leave nor convalescence should be granted to venereal patients when discharged from hospital.

Locality of Hospitalisation for Syphilitics.—As a general rule, they should be sent into hospital as near their military post as possible.

A syphilitic soldier should never be evacuated from the Front to the interior, except in the case of serious complications. It is important to keep him close to his regiment, so that, directly the treatment is finished, he can rejoin ; instructions are positive on this point, and there is no necessity to justify them.

Even in the interior, the patient should be kept as near his centre or depot as possible.

But, along with this rule, another element must be taken into consideration : the necessity of seeing that the patient is given thorough treatment, *i.e.* he should be placed in a medical centre supplied with all requisite resources, not only in material installations, but also as regards a competent medical staff.

No matter what one may think, the diagnosis and treatment of syphilis necessitate an adaptation of material and staff in order to be carried out with a minimum of expense, time, and risk.

The creation of venereological centres, or dermato-syphiligraphic centres, has been realised very happily, in the army zone, as well as in the interior.

There is no doubt that expert medical men, understanding syphilis and its treatment, may be found in all the centres, and I am acquainted with a fair number of doctors attached to regiments, ambulances, and temporary hospitals, who are capable of guaranteeing the treatment and recovery of their syphilitic patients

under the best conditions, and in whom one may have confidence. In certain cases, there may be an advantage in not removing the patient from his unit and centre, but this is applicable only in particular cases. The general rule, to which one must bow in the majority of cases, is to send syphilitic patients to hospital, or to a centre specialised for the treatment of syphilis : in the army zone, to a hospital placed in an important medical centre ; in the interior, to a special hospital clinic, or dermato-syphiligraphic centre of the region. The number of these clinics and centres cannot and should not be very considerable ; it must vary according to the regions, and may even vary at different periods, increasing if the number of syphilitics suddenly becomes visibly augmented. They should be situated in the neighbourhood of large military and hospital agglomerations, so as to reduce simultaneously the number and length of movements of the patients. Their position, however, has been judiciously settled by the military authorities, who have created sub-centres of varying number, where they appeared to be necessary.

Beyond the fact that the creation of centres and special services permits of the utilisation of competent medical men, reduces the number of similar installations and, consequently, enables them to be endowed with the material necessary for the diagnosis and treatment of syphilis, these clinics and centres have the advantage of grouping together syphilitic patients. They facilitate supervision, which must be more active than for ordinary patients, on account of the contagiousness of the disease, as well as the suppression of leave and interdiction of tobacco. In all respects, they give a far superior curative and prophylactic result than that obtained when syphilitic patients are placed in an ordinary hospital. I may add that, owing to their position near the principal places of the region, the venereological centres are able more

rapidly and completely to enlighten the medical officer of health and the commanding officer as to the variations of syphilis, the foci of contagion, and precautions to be taken in conjunction with the civil authorities for arresting their progress.

Advice to be given to Syphilitic Patients in Hospital.—The time in hospital must serve, not only for treating the patient, but also for educating him with regard to his disease and its after-effects, on the precautions he must take while in the Army and on his return to civil life.

The discussions held with the men on venereal diseases from the moment of their admission to the Army are intended to teach them how to avoid venereal diseases and learn what to do when suffering from them; but they are often forgotten when the man has become syphilitic. It is necessary now to complete and develop these, no longer by *ex cathedra* addresses, but by personal conversations with the men: in a few words, the doctor must make the patient realise the real gravity of his disease and the precautions he should take, rectifying false or incomplete ideas, frightening men who are too indifferent, and reassuring those who have got an exaggerated idea of the gravity of syphilis and its after-effects. The medical man in attendance is thus endowed with a duty of the highest importance, both from a humanitarian and social point of view, which belongs to him alone, and in which he can give full play to his concern for the welfare of his patients and of the public.

In order to facilitate this individual instruction, and at the same time impress it upon the patient's memory, the majority of syphilologists have for a long time written and distributed among their patients a short pamphlet, giving the general rules for the treatment of syphilis, and the precautions to be taken to avoid transmission. The circular of September 25th, 1916, advises that these pamphlets should be given to

syphilitics leaving special centres, and discussed with them. They are printed on a sheet of strong paper and can be kept in the pocket-book as a guide for patients. It is my custom to give one to the patient when I examine him for the first or second time; I ask him to read it, and, at a subsequent examination, it is discussed and explained to him either by me or by one of my students.

It is useful, when discharging the patient, to give him a written statement indicating the symptoms from which he has been suffering, the treatment he has received (drugs used and doses), and the dates of admission and discharge. These data may be put on a simple sheet of strong paper, which the patient is asked to keep and show whenever he has to consult a doctor. Further, they ought to be reproduced on his hospital card and on his medical case-sheet.

At the time of leaving hospital the doctor must not fail to remind each patient individually of the necessity of continuing treatment, of reporting to his regimental doctor the moment he notices a symptom of any kind, and, even if there are no symptoms, to consult him from time to time, so that his condition may be overhauled and the necessary drugs given.

The circular of September 25th, 1916, advises, further, that cutaneous patients should be ordered to have ambulatory treatment, which they must follow, and recommends that only drugs should be prescribed which soldiers are certain of obtaining easily, especially at the Front.

Post-hospital Treatment and Supervision

The syphilitic who returns to his unit after hospital treatment must be kept under observation by the regimental doctor.

In order to do this, it is necessary that the latter should have precise knowledge given by the medical

man in attendance. In times of peace, military doctors, instead of giving the diagnosis of syphilis, merely write on the hospital card the number which, in the nomenclature of diseases established by the public health service, corresponds to syphilis (No. 45): 45 *a* primary syphilis; 45 *b* secondary syphilis; 45 *c* tertiary syphilis.

The order given on September 25th, 1916, prescribes that, when leaving any venereal hospital after ambulatory treatment or after a consultation, a sealed copy of the medical report shall be sent to the medical officer of the patient's depot, or of the establishment where he is employed. This must be carefully completed, brought up to date, and classified in the report of the venereal patients of the depot. According to these instructions, the report should follow the patient in his changes of situation, by direct and confidential transmission from one medical officer to another. As far as possible, the hospital letter must bear nothing beyond the indication of a lesional diagnosis, without etiological precision.

These orders answer one of their purposes well, that of respecting medical secrets. Indeed, in the majority of cases, they respond so well that, after the patient has left the hospital, no one has any notion of the malady for which he has been treated, least of all his company doctor. Confidential reports are misleading, and get lost in their multitudinous peregrinations.

I consider that, in the Army, where the commanding officer is responsible for the health of his men, and must take measures to prevent the propagation of venereal diseases, medical secrecy is not opposed to the fact that, at any rate in war-time, the heads of companies should be aware of the cases of venereal disease contracted by their men, and this can only be effected by the hospital card. It is their duty, as with the superintendents of hospitals in times of peace, to take precautions so that their employees shall not

divulge this secret. And, further, is this a secret, having regard to the promiscuity of camp life and of hospitals, where men confide so much to each other ?

Some men at once request the medical men not to inscribe the diagnosis on their cards : there are nearly always men who are trying to disguise their disease, so as not to be deprived of leave, who wish to obtain sick-leave, or escape later from the supervision of their company doctor.

It is indispensable that the regimental doctor should receive the instructions given in the circular of September 25th, 1916, and that no syphilitic should rejoin his company without his being advised of his disease and the treatment already received.

The doctor must, according to the order of September 25th, 1916, make " a special periodical examination of all venereal patients, and specially of those who have recently left hospital, so that contagious symptoms may not pass unnoticed, and the patients may be benefited by continuity of treatment " ; and, at the time of any change of station, the new medical officer should be given information as to all venereal patients, especially the syphilitics.

The instructions do not provide for restrictions as to leave granted to syphilitics. It would be necessary to deprive all syphilitics, especially those who are married, of leave during the whole period when contagious symptoms are most liable to recur, that is to say, during the first six months at least, of syphilis.

Munition workers should be subjected to the same regulations as soldiers in the regiments, as regards the obligation of reporting the fact to the doctor, when they have been under treatment for contagious syphilitic lesions. If there is any difficulty in getting them to submit to this visit outside working hours, it would be quite simple to replace it by a visit to one of the town hospitals or to a venereal centre. Control could easily be established.

Measures for the Purpose of preventing Healthy Men from contracting Syphilis

These measures are intended for the instruction of men on venereal dangers, on the individual precautions to be taken for avoiding contamination; for the installation of establishments for the treatment of civil syphilitic patients, and finally for the supervision of prostitution.

The Instruction of Men with regard to Venereal Danger

Lectures on Venereal Diseases.—"If I had only known that I might contract syphilis, and what it means, I should not have run the risk of catching it!" This is what every medical man has more than once heard a patient say when told that he had syphilis, or who one day showed some grave syphilitic symptom, no matter whether this was an adult who had contracted the disease in some extra-conjugal intercourse, or an adolescent affected the first time he had connection with a woman.

As a result of this ignorance of many men with regard to syphilis and the sources of its infection, anti-venereal prophylactic measures have been urged, to which more and more importance has been attached of recent years. Before the war, army doctors had received instructions to institute periodical lectures for the men, in which venereal diseases, their dangers and precautionary measures, were discussed; it has even been proposed that such lectures should be included in the educational programmes of schools and colleges.

For my own part, I doubt the efficacy of these lectures. I have seen too many men expose themselves to infection and become infected, despite the fact that serious cases of syphilis had come under their notice; I have seen too many young men, who had

been educated in the most judicious manner as regards venereal diseases, contract syphilis or gonorrhœa. Finally, I have seen too many medical students and doctors become syphilitic during their student days, or when in practice, not to be somewhat sceptical as to the results of educating young people on the subject of anti-venereal prophylaxis.

It is a particularly delicate matter to give this instruction. In an audience of young people, even when belonging to a class socially homogeneous, all have not similar ideas on sexual questions, and, in order to be both understood and useful, the teaching should be adapted to the previous knowledge of the subject, as well as to the moral tendencies of each of the audience. In an audience in which some unruly subjects may turn some expression or other of the lecturer into derision during or after the lecture, this is sufficient to destroy entirely the good effect.

Individual sexual instruction, given by a highly conscientious man with sufficient medical knowledge capable of adapting himself to the special conditions of each adolescent, such as is given in certain secondary schools, and which can be given by the father of a family, or the family doctor, is of real value in warning young people against venereal diseases; but this can only be carried out with great reserve, and, no matter how tactfully done, does not always attain its object.

In the Army it is obviously impossible to realise this individual instruction, as it means unlimited leisure on the part of the doctor. Nevertheless, the regimental doctor should interest himself in the matter. I understand, from several young doctors, that they have had the opportunity of discussing venereal diseases with their men, and, having gained their confidence, have been able to impress them with ideas from which they have derived benefit. Amongst the services which a regimental doctor may render to the Army, if he understands his work well

and knows how to mix with the men and gain their confidence, while at the same time keeping up the prestige of his authority and of his science, not the least is the prevention of venereal disease. By means of private conversations, the doctor can increase the efficacy of the lectures given to units, according to regulation orders. Often, too, when talking with subalterns at mess, it will be easy for him to educate them on venereal matters, showing them the dangers and preventive methods, and also how to take care of themselves. Thanks to the confidence he has inspired in them, they may rely on him sufficiently to come to him for treatment at once, should they happen to contract syphilis. Further, he will show them how eminently important it is to take the precautions designed to prevent contamination.

Finally, it is not as a military authority due to his position, but by moral authority, owing to the character of his scientific knowledge, that the doctor must play his part in the individual instruction of the men and the staffs on venereal diseases. This, if I may say so, is in his private capacity.

There remains his part as public instructor. Although, as I have already stated, public lectures on venereal diseases do not seem to me to be as efficacious as is generally supposed, they must be given, nevertheless, because they are according to regulation, and also may have a certain modified influence on the propagation of these diseases. All useful measures, no matter how limited their influence, must be resorted to against the scourge of syphilitic infection.

The object of these lectures, as determined by ministerial instruction, is to show men the dangers of venereal diseases, the means of avoiding them, and the necessity, if contracted, of treating and curing them.

The lecturer must show briefly, but sufficiently clearly that all may understand, the symptoms of venereal disease, their manner of onset, the signs by

which they are recognised, or by which their existence may be suspected, and also their after-effects and later consequences. He must show them that syphilis may bring in its train formidable diseases : tabes, general paralysis, arteriosclerosis, that it affects future generations, kills children before birth, and causes grave degeneration in them.

These diseases are generally transmitted by direct contact, and are nearly always of venereal origin, but they may be due to accidental contagion. Consequently, they would be almost certainly avoided if sexual intercourse were abstained from. Here the lecturer should show, especially if he is addressing recruits, that continence is never the cause of any illness or disorder, and that a man may abstain from sexual relations without any danger, contrary to the general opinion amongst the young.

He must show how dangerous women are who give themselves up to uncontrolled clandestine prostitution, such as waitressses in restaurants, etc., but at the same time he must not guarantee that controlled prostitutes can be absolutely relied upon.

He should also recommend that, no matter what women a man has intercourse with, he should use a rubber protector, or applications of ointments, etc. (see p. 688).

If, in default of these precautions, or even in spite of them, symptoms of venereal disease develop, the soldier must at once consult the regimental doctor. By doing this, he will be certain of not being punished as he would be if he waited until the disease was discovered ; he will also be sure of being properly treated ; whereas, if he follows the advice of a comrade, he runs the risk of being badly looked after, and of suffering all the consequences of the disease ; and if he goes to a quack, or to some pretended anti-venereal institute, he will, at the same time, be badly treated and spend a lot of money.

It is well to add that the treatment of syphilis should be prolonged, in order to avoid evil consequences both for the patient himself and for future generations.

Of course, the lecture must conclude with a patriotic note on the dangers of syphilis for the race, and the soldier should be told that, if he wishes to avoid giving the disease to his wife, or the sweetheart who is waiting to marry him after the war, if he wishes to have a healthy family, whose future is secured by his bravery, he must keep clear of venereal diseases.

Such are the chief points in these lectures. According to the different military centres in which they are held, recruits, units already formed, the territorial army, munition workers, etc., certain paragraphs may be amplified or cut down to suit the occasion.

There can be no question here of giving the medical men appointed for delivering these lectures more than general indications. According to the centre, the intelligence of the audience, and the knowledge he has of any local danger of contamination, the lecturer will know how to vary his effects. He must never forget, above all, that his audience is a very mixed one, completely ignorant of medical terms, and that he must use expressions capable of being understood by all, even if they are defective from a medical point of view, and, if possible, they must be graphic. Without becoming trivial, he must not forget that he must speak the language of the people who are listening to him, to a certain extent; he must call gonorrhœa "clap," and syphilis "pox" or "great pox"—and must not fail to mention that it has nothing in common with small-pox—and should call simple chancre "soft chancre."

If the lecturer can get some drawings, prints, photographs, or models representing the principal forms of venereal disease, he should not miss showing them to his audience. Whenever possible, they should be thrown upon a screen, a mode which specially

impresses the masses. All these illustrations must be very simple, and clear.

The sexual and anti-venereal education of men is not done only by word of mouth. In order that oral instruction remains fixed in the memory, it must be corroborated by some printed matter.

After the lectures, it will be necessary, if this distribution has not already been made, to give to each of the audience a brief account of venereal diseases and their prophylaxis. This should be in the form of a summary of the lectures as much as possible ; it should be enlarged more or less, in the form of a leaflet, which should be typed and copied in the office of the battalion. In default of this summary by the medical lecturer, which has the advantage of being better adapted to the needs of the unit before whom the lectures have been given, some of the pamphlets published on this subject may be distributed.

Distribution to the Troops of Pamphlets on Venereal Diseases.—Since the beginning of the war, pamphlets on contagious diseases have been printed for the use of soldiers.*

These pamphlets, which the men can read at leisure, or ask their officers or doctors to explain to them, are very useful, and the Public Health Authorities have rendered a great service by printing them.

With regard to venereal diseases, one pamphlet has been brought out by the Academy of Medicine, and another printed by the Public Health Service in a small leaflet distributed to the troops at the beginning of 1916. These instructions constitute an important weapon, and their distribution should be encouraged in every way possible. I consider that they form an indispensable complement to the lectures, and may have even a greater influence than the latter on serious

* Following out the same idea, pictorial anti-venereal propaganda are recommended, the tentative efforts already made in France deserving to be encouraged.

men with reasoning power, capable of seeking the explanation of the prophylactic measures, and may aid the doctors as an excuse and subject of conversation with the different men.

In Italy, where the anti-venereal struggle began several months before the declaration of war, and was organised with extreme care, similar notices were distributed on a large scale.* The Committee of Medical Propaganda of Milan caused them to be left in public places, in military refreshment bars at the railway stations, under cover of an envelope bearing this inscription : " Italian soldiers, if your health is dear to you, if you wish for the welfare of your family and country, read, mark, and observe the instructions contained in this envelope."

Personal Precautions

A large number of syphilitic contaminations would be avoided if the men took simple and well-known precautions at the time of sexual intercourse.

The first of these precautions consists in careful examination of the genital organs, so as to be certain that there are no excoriations or sores through which contamination might occur.

The use of a rubber protector of good quality, which is neither perforated nor has been used before, is a very great, if not an absolute, guarantee against syphilitic infection. But it is also essential that there should be neither sore, excoriation from scratching, nor parasite, such as the pediculus pubis, on any of the adjoining regions not covered by the protector (pubis, inside of thighs).

Failing a rubber protector, it is nearly always possible to rub an ointment into the whole of the

* Pasini, " Cio che si fa nella sede del III. Corpo d'armata per la profilassi della malattie veneree" (*Giornale italiano delle malattie veneree e della pelle*, 1915, fasc. v.).

surface of the genital organs, vaseline by preference, which, by preventing direct contact with the virulent secretions, resists contagion to a certain extent.

After coitus, washing with soap and water is a useful prophylactic measure. This should be done as quickly as possible, using plenty of soap, especially over the glans and frenum. Soap is a well-known antiseptic for various kinds of parasites; the treponema of syphilis, which is easily vulnerable, does not seem able to resist it any more than Ducrey's bacillus.*

More or less concentrated alcohol may also serve for sterilising virulent syphilitic products; this is known to be the most certain and practical way of disinfecting a doctor's hands after examining syphilitic patients.

In default of soap and alcohol, continued washing with pure water or with the addition of sublimate may be done.

As the result of experiments on apes, in which inoculation of syphilitic products, followed by energetic friction with calomel ointment, remained negative, Metchnikoff recommended friction with an ointment containing 33% of calomel, as a means of preventing syphilis.

A certain number of patients having developed syphilitic chancres after using this ointment, Metchnikoff's preventive method has been denounced by the majority of medical men. Probably it merited neither this reprobation nor the value attributed to it by Metchnikoff. If used, it should be preceded by wash-

* The experiments of Giovannini ("Tentativi di disinfezione di ferite infette con pus di ulceri veneree per mezzo del sapone comune" (*Gazzetta medica di Torino*, 1898, Nos. 45 and 46) have shown that washing with soap and water acts very energetically on the bacillus of simple chancre: out of twenty-one experiments, a chancre only developed ten times. The most favourable conditions for success in washing are the superficial character of the sore (sore by abrasion) the small quantity of virus on its surface, the short time that has elapsed between infection and soaping, and prolongation of soaping.

ing with soap, of which it strengthens the action and should follow immediately upon suspected coitus.*

Ministerial circulars, dating from September 23rd, 1907, and November 16th, 1907, order that calomel ointment should be supplied to the regimental hospitals.

Creation of Centres for the Treatment of Syphilis amongst the Civil Population

For the last fifteen years, the staffs of special hospitals have treated patients suffering from syphilis as out-patients, without interning them.

In Paris, drugs are distributed on a large scale for the treatment of syphilis by the special hospitals (Saint Louis, Broca, Cochin).

The general use of mercurial injections has greatly facilitated the ambulatory treatment of syphilis. Since 1902, my colleague Brocq and I, at the Broca Hospital, have given out-patient treatment to syphilitic women on a large scale ; since then, nearly all special hospitals have added polyclinics to their departments for syphilitic treatment, by means of mercurial injections.

More recently, the use of arsenical compounds has enabled these polyclinics to render still more help, by realising the energetic treatment of syphilis, especially during the primary periods, without sending the patient to hospital. The dispensaries † attached to certain services consist of the old polyclinics, enlarged, brought up to date, and supplied with a complete staff.

Consultations on a Sunday, as well as in the evening, have made it possible for all patients, especially workmen, to be treated in an efficacious manner.

* Syphilis is not the only venereal disease against which precautions should be taken after coitus. I shall not go into details with regard to gonorrhœa, as I am only concerned with syphilis here.

† Jeanselme and Hudelo, " The Part played by the Dispensaries at the Broca Hospital in the Campaign against Syphilis" (*Bulletin de l'Académie de Médecine*, March 28th, 1916, p. 364).

Alfred Fournier specially recommended the generalisation of these centres for treatment, having demonstrated their share in the prophylaxis of syphilis, and devoted several publications to what he called *Prophylaxis by means of treatment.*

What has been done in Paris has also taken place in the majority of the large centres.

It is certain that the more establishments there are for patients, where they can be treated gratuitously, the more chance is there of their being treated. The better these establishments are organised for treatment, the more rapid will be the cure of contagious syphilitic lesions, and consequently the fewer the number of patients capable of transmitting the disease and the less the chances of contamination.

The polyclinics and dispensaries for patients who cannot, or will not, be treated in hospital, and the hospital services open to syphilitics, especially contagious cases which cannot be treated at home or whose symptoms require special attention, constitute two complementary organisations. The first is recommended, owing to the small expense it incurs, both for public money and for the patients themselves, who can continue work while under treatment ; the second has the great advantage that, while giving more energetic treatment than the first, it withdraws from circulation patients—men and women—during the period they are contagious.

These two can be created by the hospital administration without difficulty or large expense, and without legal intervention. Subjected to the same freedom of action as the hospitals, they receive the patients who come spontaneously, without any coercion from the police.

The difficulties with regard to working them are more trouble to overcome, especially in time of war.

Both military and civil authorities have realised the importance of increasing hospital resources for the

treatment of venereal patients. Their union has been genuinely fruitful, and their combined initiative has given all syphilitics—both men and women—the facility for treatment they desire, and will do so still more in the future.

Under the inspiration of two eminent hygienists, Medical Inspector General Vaillard and M. Brisac, Director of Public Assistance and Hygiene to the Minister of the Interior, M. Malvy, Minister of the Interior, and M. Justin Godart, Under-Secretary of State for the Military Medical Service, came to a perfect agreement, in March 1916, as to the necessary measures to be taken for the creation, extension, and working of the special services and of dermato-venereological consultations.

The Minister of the Interior decided on the creation of special services with dispensaries, called *additional hospital services*, in all the localities where the number of venereal patients rendered it necessary, and where it was possible. These offer all facilities to patients who have contracted these diseases, so that they may be treated gratuitously and with absolute secrecy.

These additional services, established principally in localities depending upon the hospital establishments themselves, are set up in all localities where regional military authority, in conjunction with the local civil authorities, indicate the necessity.

Owing to the paucity of civil surgeons in many localities, the medical service, when necessary, is assisted by military surgeons.

A certain number of additional services were soon organised, and enable one to establish, at the same time, their important part and the conditions of their organisation and working.

By a circular, dated May 21st, 1916, the Minister of the Interior advised the prefects to generalise the creation of these services, and, in conjunction with the Regional Direction of the Medical Service, to use

their authority with the administrative commissions of the hospitals and asylums, so that they should be set up in all necessary localities. As it concerned a service of general interest, it was announced that the State would share in the expense caused by their organisation and working.

The additional services have been created in a large number of localities outside large towns, where they have extended the services of venereology and dermatology of peace times. Their extent and resources vary in accordance with the importance of the civil and military populations.

Their working is carried out nearly everywhere by military doctors, especially by the medical men who are heads of dermato-syphiligraphic centres and sub-centres, or by others, not mobilised, in charge of prostitutes.

In some districts, the local authorities offered some opposition to the formation of these dispensaries ; but, as a rule, they have taken an active interest in the Army Medical Service.

The results appear to have been remarkable, the number of consultations having increased rapidly ; thanks to the activity of the doctors, and despite the defectiveness of certain localities, the treatment of syphilis has been installed under good conditions. It is only right here to mention that the zeal of some medical chiefs of centres, amongst whom I have pleasure in citing Dr. Pautrier, Head of the Dermato-syphiligraphic Centre at Bourges, has soon given tone and example to these assistant services.

From experience acquired, in order to facilitate the entrance of patients to the additional dispensaries, it is advisable not to confine them exclusively to venereal diseases, but to use them for both dermatological and venereal cases.

For reasons easy to understand, the additional services must be separated from the localities in

which diseased prostitutes are detained. On the other hand, however, they are suitable for the treatment of women who have given themselves up to clandestine prostitution, and having been arrested and found to be diseased, cannot, under the terms of the present law, be kept under arrest, because they do not live solely by prostitution, but to whom the police are compelled to recommend treatment.

Beyond this recruiting by administrative agency, syphilitics can only be led to the additional dispensaries by persuasion, or attracted there by the reputation of these services. Medical men may institute a useful propaganda by getting their poor patients to go there; but, above all, it is necessary that the civil authorities should make known their existence by discrete publicity; and the managers of workshops and industrial concerns should persuade their workpeople to go there, when attacked by venereal diseases.

These additional services will obtain their recruits by their work; patients who have recovered will gradually tell their fellow-workmen suffering from cutaneous or venereal disease.

It is to be hoped that, after the war, these additional dispensaries, established through necessity, will continue to carry out the treatment of venereal patients in a certain number of towns, outside large centres, where they have been generally neglected, and dissipate certain prejudices with regard to these patients.

The Supervision of Prostitution

Essentially, the additional dispensaries and gratuitous consultations only receive patients who have come voluntarily and nearly always spontaneously. They apply solely to syphilitics who know they are ill and want to be cured; they do not protect society either against syphilitics, who are ignorant of their disease,

nor against those who, knowing they are ill, do not hesitate to transmit their disease, rather than be treated and abandon all sexual intercourse.

The expression prophylaxis by treatment, which has gained renown from Fournier's great authority, is somewhat unfortunate, because it has seemed to some to constitute the only formula of the prophylaxis of syphilis. In reality, *prophylaxis by treatment*, so much praised by Fournier, *is a very incomplete prophylaxis*, realised solely by patients of good intention ; it does not reach those whose intentions are evil or who are weak-willed.

In order that a woman suffering from contagious syphilis will consult a doctor, it is necessary : (1) that she knows she needs treatment and that she can be treated at a hospital or dispensary ; (2) that she is willing to be treated.

Many women who at the present time abandon themselves to prostitution have only the vaguest notions of venereal diseases ; many of those who have gone on to the streets since the beginning of hostilities, or have yielded themselves to men at the back of a shop, have but little idea of what may happen to them in the future.

The majority are ignorant of the dangers they are running and of those they continue to run until the day when, owing to some serious or painful affection, they are unable to continue their business or are accused by one of their clients of having transmitted a disease to him.

Medical men in special hospitals know that it is rare to see an infective chancre in a woman. At the Broca Hospital, where the patients consist of women living a free life, as at the St. Louis Hospital, not one syphilitic woman out of twenty comes for consultation owing to chancre ; most of them do not think of having a doctor unless they have mucous plaques, and sometimes what a quantity of these! On hearing that

even the previous day they have had sexual intercourse, the number of men they may have infected during the last six weeks is terrible.

Despite the circulation among the people of instructions as to venereal diseases, and the multiplicity of places for treatment, the spectacle of our consultations has not changed.

The efforts made by the medical authorities in spreading these ideas and making known the existence and working conditions of these establishments intended for the treatment of venereal diseases, no matter how admirable and energetic they may be, run foul of impossibilities and only succeed in reaching some factory girls.

Therefore, we cannot count absolutely on the goodwill of diseased women with regard to treatment. In order to thoroughly realise the prophylaxis of syphilis by the treatment of syphilitic women, *persuasion, together with the spontaneous entry into hospital, is insufficient.* Something more is necessary.

Since the authorities have considered the subject of the propagation of venereal diseases, they have tried, by means of police measures, to withdraw from circulation women who are affected. From this originated supervision of prostitution, leading to the arrest of prostitutes, to medical inspection, to registration of those known to ply the trade of prostitution, or who, in order to take advantage of certain immunities resulting from registration, ask to have their names inscribed on the register of official prostitution, and finally to the periodical inspection of registered women to see if they are suffering from contagious diseases, in which case they are sent to hospital.

To this must be added the opening of licensed houses, under police supervision, where the occupants are subjected to repeated medical inspection.

These different measures have aroused numerous and diverse protests, in the name of morality, of

individual liberty, often the result of an exaggerated sensitiveness.

There is no doubt that there have been abuses in the repression of prostitution, that the officials charged with the investigations have often made mistakes, and that unjustifiable arrests have sometimes been made. All this, however, is not sufficient to prevent society from protecting itself against a disease which has a disastrous influence upon public health and the race, which has become a social danger, and, at the present time, constitutes a national peril.

It is not a question of confining women who lead an immoral life as a punishment, as if they were lepers, but of treating women who give themselves up to prostitution, and are diseased, and are liable to infect every day the men to whom they yield themselves. It is necessary that prostitutes should be subjected to medical inspection, and that all those found to be diseased should be treated, at least during the contagious stages. After these symptoms have been cured, and they have been shown how to look after themselves, they should be subjected to repeated examinations and again treated, if they are found to have symptoms.

Such, from the medical point of view, is the postulate of the prophylaxis of syphilis.

As Balzer says,* *the supervision of prostitution is the only measure which can give the immediate results* which it is necessary to obtain in the matter of venereal prophylaxis in the Armies.

The *supervision should apply* not only to the women known by the police to practise prostitution, the registered women, but also to *those who solicit in the streets and public places*, and to those who are declared by the soldiers to be the origin of undoubted contaminations.

* "Prophylaxis and Treatment of Venereal Diseases in Time of War" (*Presse médicale*, October 14th, 1915, p. 401).

The Academy of Medicine was justified when, at the meeting on June 13th, 1916, it demanded that there should be police supervision, not only with regard to street prostitution, but also to that in public places.

For a long time there have been rules ordering a soldier to report the woman who has contaminated him. This measure has often been criticised, and the remark has been made that the statements of men are often erroneous, either voluntarily or involuntarily, that sometimes they knowingly denounce women who have nothing to do with their disease. Despite these mistakes, which are less frequent than has been stated, the men's declarations are often most useful in acquainting the police with women who disseminate syphilis. These declarations are made under the control of the regimental doctor, who must himself question the soldiers and specify the disease from which they are suffering, as was again ordered in the circular of September 25th, 1916. They must be transmitted to the local police, who must supervise and, whenever possible, cause the incriminated women to be examined.

In the *army zone* syphilitic contaminations occur, as I have shown, from nearly all classes of women who are there, especially those who trade with the soldiers in some form or another.

To be efficacious, supervision should apply to *all* women who may be suspected of yielding to men. This is the easier because there are but few women living in this zone, and all are known to the military authorities. It is due, not only to the military authorities, but also to the police of the zone, to take the necessary measures, and the medical department must see that they are carried out by the military doctors.

In the *rest zone*, contamination originates with women who live habitually in the country, as well as numbers of others attracted there by the presence of the soldiers. Prophylactic action should apply to one as much as to the others. It is the duty of

both military and civil authorities, and can only be efficacious on condition that there is a close understanding between the two authorities. Here, again, the military doctors are the ones who have most frequently to guarantee the medical part of the service.

At the *base*, the great majority of contaminations are due to women on the streets and servants in restaurants and public-houses. Supervision should be given in the streets, especially around the stations and near the factories when the workmen are leaving; but not only on the large boulevards, as in peace time, and at night-fall, but at all times and in a very large number of streets. This supervision must not be exercised solely on women known to the police.

Borne * says, with regard to police supervision in Paris since the war: "The public authorities have moved, and the prefecture of police has given orders, to arrest girls and their bullies around the stations; but, as figures would be necessary to satisfy public opinion, special brigades have assembled the registered women well known to them. These, according to the authority of the prefecture of police whom we consulted, are contagious in the proportion of 10% only, for the inspection and prophylaxis of licensed women have continued to be enforced rigorously and regularly during the war, so that there are 90% of healthy women subjected to each drive."

Two words only on the question of *licensed houses*.

Although the security they give to their clients is only relative, and syphilitic infection is not rare in them, these establishments, when well supervised, play an important part in the prophylaxis of venereal diseases.

It is necessary that they should be visited frequently and unexpectedly. With the afflux of clients the war

* Borne, "Hygiene of the Soldier on Leave in Paris. Prophylaxis of Contagious Diseases" (*Paris médicale*, August 12th, 1916, p. 133).

brings them, both in the army zone and at the base, these visits must be made daily, as required by the Academy of Medicine. It is imperative that the medical men in charge should have at their disposal a sufficiently lighted place for examination, and the necessary instruments. The co-operation of the military doctors is to be counted on in all localities where the absence of competent civil surgeons renders it useful.

In the Manchurian War the Japanese installed free licensed houses, subjected to regular medical visits, and attributed to this the very small venereal morbidity of their Army; whereas, with the Russians, the number of venereal patients was very high.

In the Italian Army, which was supplied with licensed houses during the Syrian War, the Powers have organised licensed houses even in the localities near the Austro-Italian Front.

To return to *free prostitution*.

When a woman is known to be a regular prostitute, has been arrested several times, and is suffering from contagious lesions, when, above all, these lesions have recurred after a preliminary treatment, or she has not been treated after being warned, she should no longer be advised, but *compelled to have treatment*. In these conditions, according to the custom in Paris, she must have her name inscribed on the list of prostitutes, and be subjected to all the obligations necessitated *by registration*.

Registered women, at their own request, or as an administrative measure, must be subjected to regular and frequent medical examination. In Paris they are expected to present themselves at the Prefecture of Police for a medical inspection twice a month, on dates of their own selection. This periodicity is altogether inadequate: the security given men who have relations with women of this class is never more than relative; it is almost nil with bi-monthly visits.

These should take place at least twice a week if real prophylactic results are to be obtained. Any woman found to be affected when examined should be at once sent to the place where prostitutes are treated, and, as I have already mentioned, this should be independent of the additional hospital services, There she will be treated actively, and not discharged until the contagious symptoms have disappeared.

The "registered" women, known to be syphilitic, are given a card of a special colour in Paris, and obliged to submit, during two years, to a weekly inspection. All facilities for being treated should be given them, by means of consultations at the additional hospitals.

For the execution of such measures, the collaboration of both civil and military authorities is necessary. In all localities where the paucity of civil surgeons does not allow regular examination of prostitutes, instructions were given on September 25th, 1916, ordering the army doctors to participate in this service. In the army zone, by regulation, the commanding officer may order a military doctor to assist in examining the women in question, when this examination is made by a civil surgeon.

In the army zone, the majority of these measures relative to the supervision of prostitutes are carried out, owing to the power vested in the commanding officer.

The same applies to a certain number of inland towns, where the collaboration of a venereal specialist, an energetic medical officer of health, a prefect understanding his hygienic mission, and a municipality stripped of prejudice, has enabled all desirable measures to be taken, and the result, in all these towns, has always been a reduction of venereal contamination. In very many localities in the rest zones and in the interior, there is still much to be done, and it is necessary that measures should be taken.

They can only be effected, at the present time, by

the good-will of the municipalities, who hold the necessary powers for the order and execution of the medical regulations.

Consequently, for local reasons, some municipalities, not having sufficient understanding of the present necessities and of the interest of the whole nation, hesitate or refuse to regulate the supervision of prostitution.

Some have judicial scruples and do not consider that they are authorised to make the necessary arrests. The question of legality appears to be decided by jurisprudence.

As a matter of fact, in February 1915, the Minister of the Interior announced to the prefects and mayors that the Court of Appeal recognised that the municipal authority had the right to enter the names of clandestine prostitutes on the police register and to compel them to submit to medical inspection, including the interdiction of soliciting, or even of gathering around certain public establishments.

The mayors may, therefore, take the most important of the necessary measures ; in default of their initiative, or in the presence of their inertia, the public authorities must not remain disinterested, and it is urgent that, wherever this is necessary, the prefects may take this problem in hand and, with the authority they possess, enforce the necessary regulation.

In Italy,* where for years the relative liberty of prostitution, due to the "Crispi regulations," favoured the considerable extension of syphilis, and where rational measures were taken at the beginning of the campaign, the Minister of the Interior, supported by a decree of the Lieutenant-General of the Kingdom, did

* Balzer, "Anti-venereal Prophylaxis by Civil and Military Administration" (*Presse médicale*, January 13th, 1916, p. 10). Clement Simon, "Report presented to the Minister of the Interior and the Under-Secretary of State for Medical Services on the Anti-venereal Prophylactic Organisation in Italy" (*Annales des maladies vénériennes*, October 1916, p. 577).

not hesitate to write on September 11th, 1915 : " Prefects henceforth may adopt the strictest and most rigorous measures, even sacrifice of the principle of individual liberty, in the public interest."

If administrative authority does not consider itself sufficiently armed for the combat against the propagation of syphilis by repressing prostitution, it is necessary that it should be reinforced.

The superior interest of public health has already caused the intervention of legislation, by ordering anti-variolic vaccination, and, a short time before the war, anti-typhoid inoculation, measures the efficacy of which has been happily demonstrated by the disappearance of small-pox and the considerable diminution of the number of cases of typhoid fever. This interest is no less compromised by the propagation of syphilis, which, as I showed at the beginning of this book, is a present, as well as a future, menace to the country. *It is time that measures were taken to check this propagation.* It is the duty of the public authorities, the legislators if necessary, to take *all* the requisite measures, even should they require, for the benefit of the community, the restriction of individual liberty. The regular supervision of prostitution and its repression are necessities, both at the present time, and after the war. Every one must bear his responsibility in this question, without any regard to secondary considerations, political or otherwise.

SECTION IV

THE ABNORMAL FORMS OF TETANUS

THE ABNORMAL FORMS OF TETANUS

PART I.—THE KNOWN ATYPICAL FORMS OF TETANUS

THE various manifestations of the tetanic infection permit of the differentiation of a great variety of clinical forms.

According to the development of the disease, the predominance of certain indications, the etiology of the case, and its severity, we may describe a whole series of individual forms.

Many of these fall under the heading of the classic tetanus, and do not constitute atypical forms. Thus, for example, the super-acute forms of tetanus are merely a particular modality of the disease dependent upon the gravity of the symptoms immediately after their appearance. It follows, therefore, that sphlancnic tetanus is not, properly speaking, an atypical form. We shall mention it only, without enlarging upon it, for if the contractions are not generalised the cause is to be found principally in the very rapid development of the disease and its fatal termination within twenty-four to forty-eight hours.

On the other hand, cephalic tetanus is a truly atypical and partial form of the infection ; we shall accordingly examine its four varieties, which are :

1. Cephalic tetanus without paralysis.

2. Cephalic tetanus with facial paralysis.

3. Cephalic tetanus with paralysis of the motor nerves of the eye.

4. Cephalic tetanus with paralysis of the hypoglossal.

Having examined each of these forms, we shall terminate this chapter by a rapid summary. We propose in this to show that the varieties of cephalic tetanus are merely modifications of the clinical type first described and definitely isolated by Rose, who contributed a masterly study of the type to Pitha and Billroth's manual.

SPHLANCNIC TETANUS

Sphlancnic tetanus may be regarded as a partial form of tetanus in this sense, that death usually occurs before the contractions are generalised.

It is characterised essentially by the involvement of the muscles of deglutition and respiration, which explains the intensity of the dysphagia observed (a symptom which at the outset might lead us to suppose that we had to deal with a severe angina), by the intensity of the hydrophobia, and the crises of suffocation due to spasms of the glottis and of other muscles of the respiratory system. The dyspnœa is very marked, and the asphyxial phenomena rapidly become menacing.

From these indications it will be understood that the forms of non-paralytic cephalic tetanus which may or may not be accompanied by accentuated dysphagia or hydrophobia are to be regarded as coming under the heading of sphlancnic tetanus.

The contractions of the muscles of deglutition and respiration are accompanied and sometimes preceded

by a short interval of trismus and stiffness of the neck. This is, in short, a form of partial atypical tetanus, localised in the muscles of deglutition and respiration, and the muscles of the head and neck.

The prognosis is grave, and almost always fatal.

The development is very rapid, and death occurs within twenty-four to forty-eight hours.

This form of tetanus usually follows a visceral infection.

Its period of incubation is usually long: eight or ten days, or sometimes more.

CEPHALIC TETANUS

Cephalic Tetanus without Paralysis

Certain writers have seen fit, wrongly, as we think, to multiply the forms of cephalic tetanus, basing their classification either on the development of the disease, or on its degree of severity, or on the group of muscles affected by the contractions. Thus acute, chronic, continuous, remittent, pyretic, apyretic, analgesic, hyperalgesic, ocular, cervical, masseteric, generalised, localised, dysphagic, hydrophobic, œsophageal, and other forms have been described. It must, however, be recognised, if the numerous observations of cephalic tetanus be analysed, that clinical varieties exist which are plainly defined not only by the objective indications, but also by the progress of the disease, and by the prognosis. It is therefore impossible, save at the cost of lucidity, to include in the same description the true hydrophobic tetanus with its alarming paroxysms of dysphagia and respiratory troubles, provoked by the mere sight of a glass of water, and without any paralytic phenomena, and the varieties of tetanus with facial

paralysis or paralysis of the motor nerves of the eye.

We shall therefore describe, under the head of the non-paralytic forms of cephalic tetanus, in addition to the simple cephalic variety, characterised only by trismus and contractions of the muscles of the face and neck, the dysphagic types, which may vary from a simple difficulty of deglutition to hydrophobia.

1. Simple Cephalic Tetanus.—In this rare form of the disease the infection is confined to the cephalic region, as a result, most frequently, of a wound in the head. It is accompanied only by unilateral or bilateral trismus, or by contractions of certain muscles of the facial or even of the cervical region. But in this type there are *never dysphagic or paralytic symptoms.*

2. Cephalic Tetanus of the Dysphagic Type.—Eliminating those cases in which there is simultaneously dysphagia and facial paralysis, we may clinically define two types, which are sometimes, however, combined. These are:

The purely dysphagic form.

The hydrophobic form.

(*a*) *Dysphagic Form.*—Although this variety differs definitely from the hydrophobic form in highly accentuated cases, this is no longer the fact in cases of generalised tetanus. In such cases the respiratory symptoms make their appearance, and hydrophobia becomes the second stage of the infection. Insensibly the disease passes from the dysphagic to the hydrophobic variety.

However this may be, this form is characterised by a pharyngeal spasm which precedes the trismus, or is associated with it. The trismus, at the outset, is unilateral. The patient is sensible of pain and tension on

one side of the jaw, the side corresponding to the wound. This tension presently becomes a continuous contraction, with convulsive paroxysms. The trismus remains thus unilateral for a variable period, usually four to five days ; but as a rule, when the patient seeks advice, the indications have become threatening and the trismus is complete.

The trismus is almost invariably accompanied by cervical opisthotonos. This may be present in any degree, from a mere stiffness of the neck to the retroversion of the head. It makes its appearance shortly after the trismus. Paroxysms of the affected muscles may be aroused by the slightest excitation, such as touching the wound (Charvot), but their most frequent cause is the voluntary or spontaneous separation of the jaws.

The pharyngeal spasm causes more or less accentuated dysphagic disorders, which attain their maximum of intensity in the hydrophobic form. The patient can swallow no food ; and the least absorption of liquid sets up painful spasms of the pharynx.

Generally speaking, however, the disorders of deglutition are, more often than not, of no great severity.

Apyrexia is the rule, at all events at the outset. The temperature will rarely exceed 100·4° F.

Lastly, in addition to the cardinal symptoms, dysphagia and contraction of the muscles of the neck, we sometimes observe an intense dyspnœa, which contributes to the seriousness of the prognosis of this variety of atypical tetanus.

(*b*) *Hydrophobic Form.*—This is a very rare and exceptional form, and Réclus, on studying all the observations of cephalic tetanus, discovered only two in which a true hydrophobia was present.

In addition to the phenomena of dysphagia, and the

muscular contractions, there are alarming convulsions, provoked, in the majority of cases, either by touching the pharynx, by a movement of deglutition, or even by the mere sight of a liquid, or the utterance in the patient's presence of a phrase or word having reference to drinking.

These paroxysms manifest themselves by violent convulsive spasms, the initial seat of which is often the wound, with irradiation into the muscles of the face (masseteric or other), the neck, and the pharynx, occasionally attaining even the diaphragm; when contractions of the respiratory muscles occur, with dyspnœa and asphyxial phenomena.

Moreover, generalisation of the tetanus is frequent in this form, and the prognosis is almost invariably fatal. Even in the absence of generalisation the asphyxial phenomena and inanition may determine the fatal issue of the case.

Cephalic Tetanus with Facial Paralysis

This form of tetanus, described by Poan de Sapincourt as the facial form of the disease, had already been remarked by Rose. It is the most frequent form, and we therefore propose to study it at greater length than the others, basing our remarks on the highly interesting and fully documented thesis of Poan de Sapincourt. This variety arises from one cause only: a wound in the face or the neighbourhood of the face. It is characterised by:

1. Contractions which usually commence in the masticatory muscles of the wounded side (unilateral trismus), often invading the other side, and the musculature of the neck. They may become generalised.

2. Disorders of deglutition, of much less importance than in the preceding forms.

3. A facial paralysis, almost always localised on the side of the wound (facial hemiplegia), or, when the wound is situated on the median line, a paralysis of both sides (facial diplegia).

History

This form of tetanus has been known for some forty years, and was for the first time described by Rose, in 1872. In the two observations recorded by this writer the tetanic contractions resulted from a wound of the face; and in both patients Rose was struck by the appearance of a muscular paralysis of that side of the face on which the wound was situated.

He described the clinical aspect of the malady, and carefully studied the three cardinal symptoms:

1. Wound in the region of the cranial nerves.

2. Appearance of facial paralysis, most frequently on the injured side.

3. Tetanic contractions extending from the masseter to all the facial muscles, the muscles of the neck, and the muscles of the pharynx and the œsophagus.

Numerous observations have been recorded since the date of this first essay, and in 1888 Villar summed up the whole question in the course of a general survey.

Two years later, in 1890, appeared the thesis of Dr Albert (of Lyons); following which fresh observations were published, and Janin, in his thesis (1892), referring to two personal observations, returned to the subject, dividing tetanus, according to the predominant localisation of the tetanic toxin in the nervous centres, into medullary tetanus (generalised tetanus) and bulbar

tetanus (cephalic tetanus with paralysis of the facial muscles).

In the same year Landouzy cited a case in which there was only an appearance of facial paralysis. Réclus reported some personal observations in 1893, and in the following year Houques published his third thesis, entitled *Cephalo-paralytic Tetanus*, in which the writer made mention of no fresh facts, but, from the pathogenic point of view, put forward a theory of indirect origin. He admitted an original lesion by contusion of the terminal branches of the trigeminus against a resisting plane (osseous or external), the tetanic infection being said to invade the facial nerve, after first invading the bulb, in which the facial and masseteric nuclei are adjacent. Observation followed observation, and in 1896 appeared the last thesis of Le Dard, which dealt particularly with facial paralysis in tetanus.

Finally, we may mention the observations of Crouzon, Bourgeois, and Lortat-Jacob, the latter inspiring the work of Poan de Sapincourt (1904); and then the case observed by Binet and Trenel, in connection with which these writers briefly summarised the question of the cephalic forms of tetanus.

Etiology, Frequency, Age, and Sex

Cephalic tetanus is a rare affection, whose general etiology is that of the classical tetanus.

It must be remembered that this facial form of tetanus never occurs except as the result of a wound of the face, whether external or internal, in the region innervated by the facial nerve. This feature, according to Poan de Sapincourt, is pathognomic.

In considering the special etiology of this form of the

disease we must again note the connection between the facial paralysis and the position of the wound, since in the majority of cases the facial hemiplegia is found on the side of the wound by which the infection has entered. And, when the wound is median, there is facial diplegia.

As in the classical tetanus, men appear to be more exposed to the disease than women. Age appears to exert a certain influence, for this atypical form of the disease has been observed more particularly in youth and maturity, although it has been encountered at all ages.

We shall not further insist on the rôle of the seasons, or of professional factors, in the etiology of this form, for all that might be said would apply with equal force to the classic forms of tetanus.

Clinical Survey

Insidious in its onset, rather tardy in establishing itself, treacherous in its progress, and, owing to its complications, involving a slow recovery or a somewhat speedy death—such, in a few words, are the general characteristics of the facial form of the tetanic infection (Poan de Sapincourt).

Following a wound in the face, insignificant in the majority of cases, and caused by a fall on a stony road, or the bite of a horse, or a bullet wound, or even by a neglected ulceration, and after a period varying from two to twenty-two days (on an average, eight days) during which there are no premonitory symptoms (neither fever, nor fatigue, nor shivering, nor pains, nor insomnia) announcing the onset of the malady, the patient awakes one morning with a stiffness in one or both jaws. Sometimes there is pain at the same time.

Difficulty of mastication and of speech follow.

Presently this stiffness and constraint give way to muscular contraction and spasms, and the characteristic trismus makes its appearance. At this period the wound in which the toxins are produced is usually cicatrised, and the patient, no longer regarding it as of any importance, calls the attention of the physician only to the pain and the trismus.

These symptoms then increase in intensity, and the patient is obliged to take to his bed. The opposite side of the face may become contracted, and the wounded side is completely paralysed. We have to deal with a typical facial paralysis, the mouth crooked and drooping, allowing the saliva to trickle out ; the labial furrow is effaced, the cheeks are flaccid, wrinkles have disappeared, and the eye is widely opened.

Contracture and paralysis, moreover, are frequently associated, and the patient's face assumes the hideous mask described as the *risus sardonicus*.

The paralysis alarms the patient, while his attention is centred upon the persistence and increase of the pains, which become unendurable, the closing of the jaws, which become more and more firmly shut, the insomnia, and the prospect of no longer being able to take food. Indeed, the absorption of liquids is already difficult, and gives rise not only to pain but to paroxysmal contractions. For this reason the patient, when the paroxysm is over, fearing its return, finally refuses all nourishment.

The clinical picture is sometimes completed by dysphagia ; at each attempt at deglutition the contractions occur, and may even lead to an actual hydrophobia.

These local symptoms having fully developed, the

malady progresses slowly in the direction of recovery, or else the contractions may become more or less rapidly generalised, the local atypical malady henceforth assuming the aspect of the classic, generalised form of tetanus, with its serious prognosis.

Such, in its most frequent form, and briefly described, is the clinical aspect of cephalic tetanus with facial paralysis. We propose now to insist yet further upon the individual signs of this type, in order that we may clearly demonstrate its characteristics.

Individual Signs of Cephalic Tetanus with Facial Paralysis

1. Situation of the Wound.—We think it as well again to call attention to the fact that this facial form of cephalic tetanus has *never* been observed save as following upon a wound of the head, though, as Poan de Sapincourt has justly remarked, this does not mean that every wound in the head infected by Nicolaïer's bacillus will result in facial paralysis.

Moreover, in all the observations published one is struck by the far from extensive and occasionally superficial localisation of the wounds in which the tetanic infection has originated.

They are situated more particularly on the upper or lower border of the orbit, the superciliary ridge, the root of the nose, the malar region, or the inferior portion of the frontal region. In one single case the wound was occipital. In short, the traumatic lesions are situated in the area innervated by the two branches of the facial nerve, and above all by the superior division of the facial nerve, and Villar has given to this area the name of the orbito-naso-temporo-malar

region, thus summarising the common localisations of the wounds which give rise to cephalic tetanus.

2. Incubation. — The period of incubation is not accompanied by any indication which leads us to suspect probability of local tetanus. The wound, as a rule, becomes cicatrised in a normal manner, unless, as is often the case, it contains some foreign body. This phase lasts, on an average, nine days, but it may be shorter.

The first symptoms have been known to appear at the end of two days. Sometimes the period of incubation is longer ; it may be as long as twenty-two days.

During the period of incubation slight pain in the neighbourhood of the wound and in the temporo-maxillary articulation may be sometimes noted. Once the period of incubation is over the characteristic signs make their appearance with some degree of suddenness.

3. Trismus.—This symptom is almost always the first to appear. Sometimes isolated, sometimes associated with facial paralysis, it is occasionally accompanied by dysphagia or dyspnœa.

The trismus is confined, at the outset, to a transient discomfort in the jaw. Pain is felt upon pressure in the masseteric region, or when the patient attempts to open his mouth. The trismus is at this stage unilateral, and is situated on the same side as the wound, but it very soon becomes bilateral, although it remains predominant on the wounded side.

There is nothing surprising in this initial localisation, for we have learned experimentally that the contracture always makes its first appearance in the muscles neighbouring upon the place of inoculation.

4. Muscular Contractions.—These rarely appear before the trismus, or simultaneously with it. They are usually observed afterwards, and may invade all the muscles of the face, and neck.

They may be situated on the same side as the facial paralysis, or on the opposite side, or even on both sides (in the case of a median wound), but in general they commence on the paralysed side.

The contractions are variable in degree ; they may amount to a mere stiffness, or in very marked cases they may cause the immobilisation of the head in an unnatural attitude, giving rise to cervical opisthonotos.

As in the classical form of tetanus, these contractions are tonic, but spasmodic paroxysms may be aroused by the slightest excitation (touching the wound, or movements of mastication or deglutition).

We can understand the difficulties of the clinicians when confronted by a lesion of the facial nerve producing paralysis and contraction in *the same muscles.*

Nevertheless, it is possible to explain this phenomenon : for the paralysis and the contractions do not act in the same direction, nor in the same nervous territories. As Pechoutre contends, contraction is a phenomenon which has a central point of departure, while paralysis, at least in the beginning, results from a change in the peripheral nerve branches neighbouring upon the wound, due to the tetanic toxin (Roux, Borel, Marie, Morax).

These two symptoms have thus been explained by Guiffré, and his explanation is very probable: "The contractions of the facial muscles affected by paralysis," he says, " do not in this case differ in any way from the ordinary tetanic contractions, except that they occur in muscles already paralysed. To explain this fact we

may suppose that the voluntary impulse is not sufficiently transmitted by the affected nerves to the muscles of the periphery, while the tetanic toxin, on the contrary, is sufficiently powerful to sur-excite the nuclei of the facial nerve, and to cause contractions in muscles which no longer react to the voluntary impulses."

Guiffré goes so far as to compare tetanus to electrical stimulation, which is able to cause contractions of paralysed muscles.

In those cases in which there are only paralytic phenomena, it must be supposed that the tetanus toxin has remained localised at the periphery, and has not reached the nucleus of the facial nerve, or has not affected it sufficiently to excite the paralysed rami.

We have also mentioned, and this fact is recorded in a score of observations, and particularly in those of Charvot, Villar, and Réclus, that the contractions may occur on the opposite side to that affected by the facial paralysis. The result is a very remarkable facial asymmetry, which gives rise to the grimace known as the *risus sardonicus*, when the paralysed side assumes an expression of profound apathy, while the contracted side wears an expression of appalling fury (Poan de Sapincourt). This characteristic expression is peculiar to the tetanic infection.

The contractions may also become generalised; cervical opisthotonos often accompanies cephalic tetanus. But if the infection gains ground the contractions may affect the trapezius, and the muscles of the back, abdomen, and limbs.

This extension is serious, above all when the pharynx, œsophagus, and diaphragm are in turn affected, as dysphagia may be caused, and consequently inanition and asphyxial symptoms.

5. Facial Paralysis.—Complete or incomplete, facial paralysis is never absent in this atypical form, although paralysis is extremely rare in the classic form of tetanus.

Commencement.—Facial paralysis is not always the first sign of the malady, and we have seen that trismus may precede it or co-exist with it. Nevertheless, it is an early symptom, which at once attracts the attention of those about the patient, and of the physician.

It is most frequent between the seventh and the twelfth day, but may appear, as we have remarked, at any time between the second and the twenty-fourth day of the disease. In cases likely to recover it tends to appear late, while in fatal cases it makes its appearance between the second and eighth days. Its early or late appearance may, therefore, be of prognostic significance.

Lastly, there is no fixed relation between its appearance and that of the trismus; sometimes paralysis follows the latter; sometimes it appears simultaneously; sometimes it precedes it.

Situation.—As a rule the facial paralysis is observed on the same side as the wound in which the tetanic toxin is produced, and if the wound is median, there is usually facial diplegia, either as an initial or as a late symptom.

Clinical Characters.—The facial paralysis occurring in cephalic tetanus recalls in every respect the ordinary paralysis of peripheral origin. Nevertheless, when the tetanic toxin has invaded the nervous centres, when the intraosseous portion of the facial nerve is injured, the paralysis presents the characteristics of a central paralysis of bulbar origin.

In the super-acute forms, moreover, it may resemble bulbar paralysis from the beginning, and in this case

there is nothing surprising in the development of a paralysis of the side opposite to the wound.

This is a paralysis of a toxi-infectious nature, comparable to the paralysis of diphtheria.

(*a*) The type most frequently observed is cephalic tetanus *with complete peripheral facial paralysis.* Into this group fall those cases in which the paralysis affects one half of the face, and involves all the muscles innervated by the two branches of the peripheral facial nerve, the motor nerves of the muscles of the ossicles or the chorda tympani never being affected. Such cases present the type of the ordinary peripheral facial paralysis. In all the observations of these cases we find the signs of this affection are more or less fully recorded. There is exaggeration of the facial asymmetry by every movement, the disappearance of the naso-labial furrow on the affected side, and on the sound side there is incomplete closure of the lips, with dripping of saliva, and the nose is diverted to the sound side. The ala nasi on the paralysed side is no longer raised each time a fairly deep breath is taken, but, on the contrary, is flattened, and the nostril contracts, while the eye on the affected side can no longer be closed ; sometimes this gives rise to epiphora and conjunctivitis. The wrinkles of the forehead are effaced ; the superciliary muscles are immobile ; and the face is strange and expressionless.

Sweating on the affected side is found to be affected on application of the pilocarpin test.

In this complete form hearing and taste are unaffected, the soft palate is normal, and the uvula is not drawn to one side.

(*b*) In certain cases the superior facial nerve is unaffected, and consequently the superior facial muscles

are not involved. The eye may be closed, and the lines and wrinkles of the frontal region are not obliterated.

In this variety we have to deal with an incomplete facial paralysis involving the lower facial muscles, and this in turn may be divided into two categories, accordingly as the middle rami only or the inferior rami only of the facial nerve are affected. It is thus possible to define a middle inferior type and a pure inferior type, a good example of which is described by Crossonard. In this case, a wound of the lower lip, only the triangularis menti muscle was affected.

(*c*) Much more rarely, and quite as an exception, the toxin may spare the *inferior facial region*: we then have *cephalic tetanus of the superior facial type*. The eye is open, and the wrinkles of the forehead are effaced, but the muscles of the nose, lips, and chin are unaffected.

(*d*) Lastly, there are cases of *total facial paralysis* no longer peripheral, but involving the muscles of the ossicles and of the chorda tympani. In these cases there is a toxic invasion of the petrosal portion of the facial nerve, which is manifested by disturbance of the hearing, taste, and smell. The observation recorded in 1902 by Lortat-Jacob is very interesting and instructive in this connection; the patient, who was ten years of age, had received a wound on the outer portion of the orbital rim of the left malar. On the eighth day cephalic tetanus made its appearance, with complete facial paralysis and disturbances of smell, taste, and hearing. Odours could not be perceived by the left nostril (the paralysed side). Taste was abolished on the same side; antipyrine, sulphate of quinine, and sugar (syrup) failed to produce any plainly different sensations, while taste and smell on the right-hand side remained unaffected.

A watch was heard at a distance of 30 centimetres

on the right side, and at a distance of more than 40 centimetres on the left side, indicating some degree of hyperacusis on the injured side.

This fortunately rare form is far more serious than the preceding types ; it indicates, as a rule, a tendency to generalisation ; moreover, the paralysis itself is less readily recovered from.

Development and Prognosis

The facial paralysis usually remains localised during the whole term of the malady. It improves and tends to disappear simultaneously with the trismus, sometimes even before the latter (Oliva).

In certain cases, however, the paralysis has disappeared only when convalescence was reached, and it has even been known to persist after recovery from active tetanus.

As a rule, when the patient has recovered from tetanus the paralysis has disappeared. Its prognosis is, therefore, good, especially when its appearance is delayed.

Diagnosis of Facial Paralysis.—When the facial paralysis is the first sign of tetanus it is difficult to recognise its etiology, and the causes of error are numerous.

Paralysis of central origin is quickly eliminated ; with this there are other symptoms of a serious lesion.

Similarly, hystero-traumatic functional disorder, as the result of a wound in the head, might possibly produce somewhat similar symptoms ; but in this case the mode of onset, and the fact that the lower face is never exclusively affected, and above all the condition of paresis rather than paralysis, makes it totally unlike peripheral facial paralysis.

We may inquire, too, whether the paralysis may not be caused by a direct traumatic lesion of the facial nerve; we may have to do with either a peripheral lesion of the nerve, a mistake easily made, considering the usual position of the wound, or a lesion of the intra-petrous portion due to fracture of the petrosa. The symptoms peculiar to this affection will rapidly establish the diagnosis.

Lastly, the physician may suspect a case of Bell's palsy, or disease of the middle ear.

Such a case may be accompanied by temporo-maxillary arthritis and unilateral trismus, which render the diagnosis still more difficult. An examination of the auditory passage should always be made.

Pathogenesis.—Basing our remarks upon experimental data, the facial paralysis may be conceived as follows:—After a superficial infected wound in the territory of innervation served by the facial nerve, there is an absorption of toxin by the peripheral nerve branches in the neighbourhood of the wound, the toxin gradually reaching to the central neuron and the medulla, travelling solely along the nerves.

The infection may be localised, or may, on the contrary, spread along the cerebro-spinal axis. It follows that we may observe different forms of paralysis according to the degree of infection.

6. Fever.—Most writers regard apyrexia as one of the peculiar and constant characteristics of cephalic tetanus. There is frequently, however, a slight rise of temperature, and fever is almost always encountered when there are indications pointing to the invasion of the tetanic infection—that is, in serious cases. In the absence of such a rise of temperature the pulse must be consulted,

for its great frequency is almost the rule in the facial form of tetanus.

Bacteriology.—In some cases of cephalic tetanus it has been possible to demonstrate the presence of Nicolaïer's bacillus, and even to cultivate it. It has even been possible to produce an experimental tetanus with local contractions (Lortat-Jacob). But in the tissues attacked by the tetanic toxin no discovery has been made of clearly defined lesions such as would explain the intensity and the gravity of the clinical indications observed.

Development, Duration, Prognosis.—As in the classical forms of tetanus, the development may be acute or sub-acute.

In two cases its duration did not exceed three days (two deaths); in fifteen cases it varied from five to ten days (fourteen deaths). In the other cases the tetanus was prolonged after the second week (one death and four recoveries).

The prognosis is thus to a certain extent dependent upon the progress of the disease, yet a case which by its early stages and its duration would lead us to expect rapid recovery may suddenly assume an acute development and end fatally. Similarly, a case regarded as mortal may terminate favourably.

The prognosis must accordingly always be reserved, whatever the course of development, or the apparent benignity or gravity of the symptoms, and although the prognosis is much less gloomy than in ordinary tetanus.

The mortality does not exceed 50 per cent.

Lastly, there are certain factors which may darken the prognosis.

Apart from the period of incubation, the progress of the malady, the degree of infection, and rapidity of

spread, the prognosis is also dependent upon the age of the individual, and his powers of resistance, and on an early diagnosis, which will permit of the speedy institution of a curative treatment.

Diagnosis.—Once typical symptoms have appeared they permit, as a rule, of a ready diagnosis. It must not, however, be supposed, because a wound in the trigeminal area is accompanied, at all events in the first place, by trismus of the same side, and by facial paralysis, that there is no room for hesitation as to the nature of the symptoms observed. Above all at the outset, when the three chief symptoms are not complete, certain affections may give rise to confusion, the more readily in that the wound may be cicatrised, insignificant, and occasionally forgotten by the patient, while the trismus may be slight, and unilateral, and facial paralysis may be late in appearing.

The tetanic infection may be unrecognised when the initial sign is merely a pain localised on one side of the face, or even a unilateral trismus. A direct traumatism of a branch of the facial nerve, the cutting of a wisdom-tooth, hysteria, dental caries, or cold may provoke the same objective manifestations.

Similarly, spasmodic facial neuralgia (tic douloureux) may give rise to analogous pains and contractions. These are frequently observed in certain cases of neuralgia of the trigeminal nerve. As a rule, there is a sudden contraction of the muscles innervated by the facial nerve on the side corresponding to the pain. This is, however, merely a motor reflex caused by the sudden pain experienced by the patient.

Lastly, the traumatic spasms described by Colles and Follin are differentiated only by the absence of Nicolaïer's bacillus.

It is, however, probable (and we shall return to this point when examining the monoplegic partial forms of tetanus) that in many of the cases described by these writers they were in reality confronted by atypical and localised forms of tetanus.

However this may be, when we have to deal with a wound in the face which may have been contaminated by the soil, or by dust, or which contains a septic foreign body, and is accompanied by local contracture, or merely by facial asymmetry, the possibility of cephalic tetanus with facial paralysis must never be overlooked. In the absence of trismus it will always be necessary to investigate the case thoroughly from the clinical bacteriological aspect before rejecting the hypothesis of an atypical tetanic infection. By careful investigation we may sometimes recognise this special form of tetanus at the outset, and institute a treatment which will be the more efficacious as it is more promptly applied.

This serotherapeutic and symptomatic treatment will differ in no respect from the treatment adopted for other forms of the disease. We will only mention that the particular localisation of the infection has encouraged certain clinicians to administer injections of antitoxin near the place of inoculation, and for this purpose the lax cellular tissue of the cheek offers as great a facility to the needle as the skin of the thigh or the abdomen. Others have recommended the irrigation of the wound with antitetanic serum; it is possible that in this method, if the serum does not destroy the toxin, it may diminish its virulence and its rapidity of production.

One thing at least is certain, and we cannot lay too much stress upon it: that when confronted by an

excoriation or a wound of a suspicious character on the face (however slight or superficial it may be) we ought always to administer a preventive injection of anti-tetanic serum, which should be repeated a week later if any doubt persists as to the possibility of tetanus, and that the wounded subject will thus be protected from the risk of a delayed infection.

Cephalic Tetanus with Ophthalmoplegia

In addition to facial paralysis, cephalic tetanus may be accompanied by ophthalmoplegia, and Worms, in his thesis on the subject, has particularly examined this form.

History

The affection of the ocular muscles in cephalic tetanus long escaped the attention of medical writers. Hippocrates, Strümpel, Larrey, and Harkness had, it is true, mentioned the occurrence of ocular troubles during tetanus, but they did not attach any great importance to the fact. Only in 1882 did Wahl publish the first observation of tetanic ophthalmoplegia. Four years later Sereins mentioned a case of cephalic tetanus complicated by ptosis, and in 1890 Rocliffe described a further case accompanied by a double ptosis and diplopia. These observations were followed by those of Roberts and Williamson in 1891, and of Marx and Caird in 1893. Then, in 1894, Fromaget published an interesting memoir in the *Archives d'Ophthalmologie*, dealing with the ocular manifestations of tetanus. After the appearance of this memoir numerous observations were published, and Worms, in 1905, in his thesis upon "bulbo-paralytic"

tetanus, described the clinical appearance of the particular atypical form which we are about to recapitulate here.

Etiology

As in the other forms, the cause of cephalic tetanus with ophthalmoplegia is the infection of a wound by the tetanus bacillus, and we may repeat here what we have already stated in connection with the preceding form as to the influence of such factors as the profession of the subject (carters, gardeners, farm labourers, etc., being particularly liable to infection), the nature of the traumatism, and the influence of the factors of age and sex (adult man).

A more important factor is the position of the wound, which is, in the majority of cases, a wound of the head, situated in the orbito-superciliary region, which, on account of its prominence, is frequently exposed to traumatisms.

The eyebrow is often involved. The skin of this region, on account of its anatomical situation, is exposed to the type of contused wounds favourable to the development of Nicolaïer's bacillus.

The eyelids are sometimes a site of infection when injured by cutting or stabbing instruments.

In several cases, those in which the tetanic ophthalmoplegia was most clearly defined, the trauma was in the eyeball.

As Worms has justly remarked, the eye, protected by the superciliary arch, and backed by a fatty cushion, would seem as though bound to escape tetanic infection. In these cases, however, the wounds were not caused by falling upon the face, but by projectiles (bullets, splinters of wood, whip-lashes) discharged so

suddenly that the sufferers were unable to protect the eyes.

It must not be supposed that tetanus occurring under such conditions is always complicated by ophthalmoplegia. The cases observed by Denuce and Chrisolm manifestly prove as much.

Lastly, when we have to deal simply with ptosis associated with paralysis of the face the position of the wound may be in the region of the cheekbone, the nose, the temporal region, or even in the mucous membrane of the buccal cavity.

A case is recorded in which the wound was in the right foot (Zack).

Clinical History

Initial Symptoms.—The ophthalmoplegia may on occasion be the first symptom of tetanus, apart from any other manifestation. This was the case in the observation published by Lépine and Sarvonat. In such cases it is only after the lapse of some days that the stiffness in the jaws and a slight amount of pain make their appearance. The patient experiences a difficulty in speaking, and very soon the stiffness passes into contractions and spasms of characteristic trismus.

The patient is then obliged to take to his bed, and the symptoms become aggravated. The face becomes contracted on the sound side and paralysed on the side of the lesion (*risus sardonicus*). The trismus becomes more and more intense and alimentation impossible. The muscular phenomena usually extend to the neck, the trunk, and the limbs, especially the lower limbs.

During this development the ophthalmoplegia persists, either unchanged or with certain modifications.

One muscle, which was not involved, may become paralysed ; another, which was completely paralysed, may begin to act again ; the strabismus may increase or diminish (Worms).

If the ophthalmoplegia is localised in one eye, then toward the last days of the malady, or sometimes only during the terminal period, the sound eye is also affected.

Symptomatology. — The ophthalmoplegia in the observation published by Lépine and Sarvonat, which we have already described, was so definite that we may well describe it. In their patient paresis of all the muscles was observed, the eyelid falling and hiding the greater part of the cornea, and the patient, who had the appearance of being drowsy, threw the head back in his attempts to see from under the drooping lid. The forehead was wrinkled and the eyebrow lifted, in order to supplement the insufficiency of the levator palpebræ. Examining the movements of the eye, it was seen to be fixed in one position ; slight movements outwards only were observed, the right-hand external muscle being less paralysed than the rest.

In Marx's patient the ophthalmoplegia was of the external type—that is, there was paralysis of the external musculature of the eye, the internal musculature being unaffected.

In the case observed by Roberts and Williamson the ophthalmoplegia was bilateral, and established itself progressively ; the left eye, situated on the side of the wound, was the first affected ; it became immobile, the pupil moderately dilated and not reacting to light. On the following day the third and fourth pairs of cranial nerves on the right side became paralysed, and the pupil on that side was noticeably contracted.

In these cases the ophthalmoplegia was total from the outset. In other cases it was at first restricted to certain muscles.

Thus paralysis may involve the whole of the muscles innervated by the common oculomotor nerve, to the exclusion of the intrinsic musculature.

The signs of a paralysis of tetanic origin of the third pair of cranial nerves offer no special character to distinguish them from the signs of ophthalmoplegia of a different origin. It must be remembered, however, that when the paralysis is localised only in some of the muscles innervated by the third pair, the *levator palpebræ superioris* is almost invariably the muscle most frequently affected. However, in the case observed by Wahl there was paralysis of the two right-hand internal muscles (divergent bilateral strabismus).

The isolated paralysis of the levator is often partial, in the sense that the patient can slightly lift the upper eyelid; but this movement must be differentiated from the lifting of the eyelid which may be effected by the compensatory action of the frontalis muscle. Occasionally the ptosis is the first manifestation of the paralysis. It is usually unilateral and most frequently situated on the same side as the wound, but it sometimes happens that the two levator muscles are simultaneously involved. Sometimes, as in Rocliffe's case, the ptosis is more accentuated on the side of the wound.

The paralysis of the sixth pair of cranial nerves is rarer, especially the isolated form. This form has been reported only on one occasion. It is usually observed in association with paralysis of the third and fourth pairs. Similarly, the isolated paralysis of the superior oblique is exceptional; only one case is known. It is

usually observed in conjunction with a paralysis of the oculomotor nerve.

The Situation of the Ophthalmoplegia.—As is the case with facial paralysis, ophthalmoplegia may be situated on the same side as the wound, but it is usually either bilateral from the first, or it invades the two ocular globes successively. Rarely the ptosis and ophthalmoplegia may make their appearance on the side opposite to the wound.

Pupillary Disorders.—Pupillary disorders may also be observed, either simultaneously with the paralysis or, more rarely, isolated.

These disorders have been noted by all the clinicians who have studied cephalic tetanus, and Albert, in his thesis, mentions that in this atypical form the sphincter of the iris is always contracted, and the pupil, greatly diminished, becomes pinpoint and does not react to light.

Possibly the condition of myosis present is due to the local action of the tetanic toxin on the sphincter of the iris.

It must be noted, however, that Jacobson has observed mydriasis in a case of cephalic tetanus. However this may be, in spite of myosis, accommodation is normal, at all events in the beginning, for later on the test becomes difficult. Moreover, Lépine and Sarvonat discovered that in their patient the iris dilated readily under the influence of atropine.

Amblyopia has also been noted (Larrey, Harkness), and according to Chevalier these amblyopic phenomena should be placed in the category of amblyopia due to intoxication without lesion of the fundus of the eye. But this is a pure hypothesis, for no ophthalmoscopic examination had been made. In those cases

in which it was possible to make such an examination, the fundus of the eye was found to be normal in four cases, and hyperæmic in the cases observed by Wahl, Fromaget, Lépine, and Sarvonat, but without other lesion.

Pathogenesis.—We shall not insist upon the different theories successively put forward in order to explain these forms of paralysis. We shall cite, as matters of historical interest, the asthenic theory advanced by Rose, and the reflex theory supported by Sereins and Houques, but the infectious theory alone appears to explain these special lesions. The experimental investigations of Brünner, Vaillard and Vincent have indeed demonstrated that the paralysis appears later than contraction, and is due to a greater virulence of the tetanic poison, or to the more prolonged action of this poison. Moreover, from the clinical point of view, the forms of cephalic tetanus which are accompanied by paralysis are particularly serious. Further, anatomical and pathological researches show that these forms of paralysis are not due to changes in the peripheral nerves, but rather to cellular lesions, and our clinical knowledge does not permit us to entertain the hypothesis of a neuritic origin. The ocular paralysis observed on the side opposite the wound can only be explained by a nuclear lesion—a theory which seems to receive general support—while the frequent occurrence of bilateral paralysis must also be due to the same mechanism. The habitual association of ocular paralysis with facial paralysis, the persistence of the pupillary reaction, the absence of blepharospasm, and the dissociated, incomplete type of the paralysis of the common oculomotor, recall the clinical features of nuclear ophthalmoplegia.

This nuclear origin is further rendered probable by the presence of facial paralysis, which, in the majority of cases, is total, and which may be situated on the opposite side to the wound.

Finally, a last argument in favour of this origin is to be found in the fact that the ophthalmoplegia may be associated with a paralysis of the hypoglossal, and numerous autopsies have led to the discovery of lesions of the bulbar nuclei, especially in the region of the facial nerves.

According to Worms, these forms of ocular paralysis are the expression of a polioencephalitis, being analogous in this to post-diphtheritic paralysis.

As to the route followed by the toxin, if we go by the experimental researches of Courmont and Doyon, Marie and Morax, Meyer and Ransom, we may consider that paralysis of the cranial nerves may occur in two different ways, but it is difficult to assert that one mode of propagation is more probable than the other.

1. **Through the medium of the trigeminal,** lesions of which upon the face are of frequent occurrence. In wounds of the eyebrow, for example, the injured supra-orbital nerve may lead the toxin to the oblongata, and the tetanic poison having infected the trigeminal, may gradually gain the nuclei of the motor nerves of the face and eyes, where it causes lesions which the microscope reveals with difficulty.

2. **Through the medium of the motor nerves of the face** (facial and common oculomotor). If the process is readily explicable in the case of facial paralysis, it is equally so in the case of ophthalmoplegia, if we suppose, with Duval and Mendel, that the fibres of the superior facial nerve which innervate the frontal muscles, the

superciliary muscles, and the orbicular muscles of the eyelids, spring either from the external oculomotor nerve (Duval) or the common oculomotor nerve (Mendel).

If, on the other hand, we remember that in most cases of ophthalmoplegia the wound has been situated in the territory innervated by the third pair of cranial nerves we may suppose that the toxin reaches the oblongata by way of a branch of the common oculomotor nerve. Finally, from the nucleus of the common oculomotor or its branches the toxin may reach the nuclei of the nerves of the opposite side.

Diagnosis.—The first question which presents itself in a case of cephalic tetanus with paralysis of the motor nerves of the eye is whether we are not confronted by a *false ophthalmoplegia*—that is, an apparent paralysis due to spasm of the ocular muscles. In this connection it is possible, as the result of a superficial examination, to confound the paralysis of the right external rectus with spasm of its antagonist, the right internal rectus.

To avoid this error Borel advises that the field of fixation should be determined by placing the eye at the centre of the perimeter, the head being immobilised. The sound eye is opened, while the affected eye is made to follow an object which is moved from the centre toward the periphery.

The field of fixation is normal in the case of spastic strabismus and limited in the case of paralytic strabismus. Borel has also discovered another means of differentiation in the graphic curve giving the excursion of the ocular movements. This curve should be contracted in the one case, and in the other case should assume a basin-like form.

In the spasm Parinaud notes supplementary con-

tractions—involuntary blinking of the eyelids, fibrillary contractions of the orbicularis, a lack of co-ordination and an abnormal suddenness of muscular movements, and even nystagmus. Moreover, while, for instance, in paralysis of the right-hand external oblique adduction is normal, and abduction suppressed, in the spasm, as in the convergent strabismus, the movements are of normal extent and readily executed. Finally the spasms are *inconstant*, while the paralysis is fixed.

Once ophthalmoplegia is recognised its cause must be sought.

(*a*) If the patient does not furnish evidence of a previous wound or traumatism, we may, to begin with, consider the possibility of a meningeal lesion, and in particular a *cerebro-spinal meningitis*. As in ophthalmoplegic tetanus, we may, in fact, observe stiffness of the neck and ocular paralysis. But in this case we discover high fever (104° F.). Although partial tetaniform cramps may be present, there is no trismus, and the masseteric contraction can be partially or wholly overcome. Moreover, in tetanus Kernig's sign is absent; in many cases, for that matter, it would be impossible to look for it, on account of the intense muscular contractions. Lastly, a lumbar puncture, and the chemical, cytological, and bacteriological examination of the cephalo-rachidian fluid will enable us to remove any doubt.

The prodromal symptoms may also assist the diagnosis. Shivering, headache, and vomiting do not accompany the silent invasion of cephalic tetanus, and while the intellectual faculties are disordered in meningitis they remain unaffected in tetanus.

The form of *tubercular meningitis* in the adult,

described by Boix, commencing with isolated trismus, may simulate tetanus with paralysis of the motor nerves of the eye. The trismus is presently followed by stiffness of the neck, and sometimes by dorsal contractions, which do not facilitate a differential diagnosis. But in bacillary meningitis there are no convulsive spasms, and hesitation quickly disappears with the advent of the entire symptomatic train of the meningeal lesion : high temperature, modifications of the pulse, Kernig's sign, and the special character of the cerebro-spinal fluid.

(*b*) If the patient exhibits a wound resulting from a previous traumatism (a fall on the head or a violent blow in that region), accompanied by ocular paralysis, we may inquire whether the ophthalmoplegia is not due simply to a *fracture of the orbit*, a hypothesis all the more possible in that wounds inflicted by firearms are liable to involve the orbital region.

Considering the probability of tetanus, this is in general due to *superficial*, localised, and insignificant wounds, which do not permit us to suppose the existence of a considerable traumatism. In the contrary event we must consider the possibility of a *fracture* with intra-orbital hæmorrhage, and the formation of a clot, which, according to its position and its dimensions, may give rise to a more or less complete immobility of the eye, thus simulating paralysis.

If the traumatism which has determined the wound on the face was of a certain severity, we may also pause to consider the possibility of a *fracture of the base of the skull*, with signs of compression. In such a case other and graver symptoms will be observed : stertor, disorders of movement, but no trismus ; all these signs, moreover, would appear at the time of the accident,

while in tetanus there is a phase of incubation lasting for some days.

If ocular paralysis following upon a wound in the face cannot be explained by a *fracture*, if the subject is nervous, presenting all the signs of a functional neurosis, it is permissible to consider the possibility of an ocular manifestation of *hystero-traumatism*.

This will seem all the more possible inasmuch as under the influence of the trauma the hysterical manifestation develops in the neighbourhood of the wound, and because in this neurosis the phenomena of spasm and paralysis are very often associated.

Parinaud, examining the ocular derangements occurring in hysteria, has shown that apart from pseudo-paralytic ptosis the hysterical muscular disorders of vision are confined almost exclusively to modifications of the associated movements of the eyes. *Paralysis involves only the voluntary movements*; the eyes may move instinctively under the influence of numerous excitations which give rise to ocular movements without the direct intervention of the will.

Lastly, *hysterical ptosis* has individual signs which enable us to diagnose it; it is not permanent, and the eye is able to open when the attention is quickly engaged; it is often accompanied by photophobia; the eyebrow, instead of being greatly elevated, is, on the contrary, depressed.

The diagnosis of cephalic tetanus with ophthalmoplegia may be extremely difficult to establish.

The clinician, confronted by a wound of the face, *even an insignificant wound*, often cicatrised, accompanied by ocular paralysis, a slight facial asymmetry, and isolated contractions, should consider the possibility of tetanic infection. He will look for trismus, and

in the absence of this sign, if there is the least suspicion of a tetanic origin, he should immediately treat his patient accordingly, without waiting for the occasionally tardy appearance of confirmatory symptoms.

Prognosis.—Generally speaking, ocular paralysis is only of brief duration, and even in some fatal cases it has disappeared before death.

It disappears either simultaneously with the trismus and the facial paralysis, or after them.

The prognosis of the ophthalmoplegia, considered apart from the other tetanic symptoms, is good, since among the whole of the cases recorded only once has it persisted for as long as three months. At the end of this period Rocliffe's patient still exhibited diplopia and a slight ptosis in the left eye.

If the prognosis is difficult to establish positively, as we have only a limited number of observations to go by, it is nevertheless noticeable that those cases in which ophthalmoplegia has been very definitely manifested have had a fatal termination.

In order to give a prognosis we must take into account the muscular contractions, the temperature, the respiration, and above all the duration and the time of the first appearance of the tetanus. Putting aside the unforeseen complications which may supervene, we may say that chronicity is a factor of recovery ; the duration of those cases which have recovered has varied from four to twelve weeks (average, seven weeks).

The prognosis is more serious in proportion as the tetanus makes its first appearance at an earlier date. Thus, in the fatal case observed by Lépine and Sarvonat, the period of incubation was five days.

This, by the way, is a prognostic factor common to all forms of tetanus infection.

The treatment of this variety is that of ordinary tetanus. We will only remark that if the ophthalmoplegia persists after the evolution of the tetanus is terminated we may employ local electrical treatment and strychnine, as for facial paralysis.

Cephalic Tetanus with Paralysis of the Hypoglossal

In the course of cephalic tetanus we may observe, in association with facial paralysis and ophthalmoplegia, a paralysis of the hypoglossal. Such observations are exceptional. Their principal interest resides in the fact that from the pathogenic point of view they argue in favour of the nuclear origin of the forms of paralysis occurring in cephalic tetanus. Clinically speaking, the invasion of the hypoglossal determines a syndrome of labio-glosso-laryngeal paralysis.

The different forms of paralysis which characterise each variety of cephalic tetanus are often found to be associated in the same patient, and there is a particular clinical type, that of Rose's "cephalic tetanus," which is characterised by three essential signs :

1. Contractions localised in the cervico-facial region.
2. The existence of facial paralysis which may attack the facial nerve, the motor nerves of the eye, and the hypoglossal.
3. An essentially chronic development, without fever, the general condition being unaffected.

We may therefore resume the symptomatology of cephalic tetanus in a fairly simple fashion : the patient complains that he cannot open his mouth, and experiences the greatest difficulty in swallowing food ; whence trismus and dysphagia. The symptoms may go no

further than this (dysphagic and hydrophobic forms). But in general the patient exhibits a more or less accentuated facial paralysis, a paralysis affecting the wounded side, a paralysis sometimes difficult to discover when there is contraction of the muscles of the opposite side of the face (Binet and Trenel). To determine whether it actually exists it is enough to instruct the patient to make an effort to open his lips or his eyelids. If he cannot do this in that part of the face which is immobile and inert, there is really paralysis of the seventh pair of cranial nerves. This is the facial form of cephalic tetanus.

Occasionally signs of ophthalmoplegia associated with facial paralysis make their appearance, dominating the clinical picture (Worms' bulbo-paralytic form). There is sometimes paralysis of the sixth pair of cranial nerves, sometimes of the fourth pair; but most frequently it is the common oculomotor which is involved. If the lesion involves only some of its fibres a greatly localised paralysis results, affecting either the levator palpebræ superioris, causing ptosis, or the motor muscles of the eye, giving rise to strabismus, or the internal musculature, causing loss of accommodation and possibly explaining the amblyopic phenomena observed in certain patients. These ophthalmoplegic phenomena may appear before the facial paralysis, the ptosis becoming the first indication of cephalic tetanus. Lastly, the hypoglossal may be affected, with the labio-glosso-laryngeal syndrome predominant (fourth form of cephalic tetanus).

Unilateral Tetanus

We do not believe that there is such a thing as unilateral tetanus characterised by the sole and exclusive

localisation of the contractions to one side of the body. These are simply cases in which the tetanic symptoms persist for a long time on one side of the body only, and remain very predominant on that side during the period of generalisation, giving rise to pleurothonotos.

Properly speaking, there is here no question of an atypical form, so we shall content ourselves with the mention of this particular variety of the tetanic infection.

PART II.—LOCAL TETANUS OF THE LIMBS

CHAPTER I

OBSERVATIONS

We shall eliminate from this variety of tetanus the cases observed by Esau, Boinet and Monges, and Curtillet and Lombard, in which the tetanic infection was not localised in the initial seat of infection during the entire development of the disease. In Esau's observation, entitled *Local tetanus of the hand*, the malady, despite the title, was local only during a first period ; contractures developed in the left upper limb seven days after a traumatism of the left hand ; but nine days after their appearance trismus and opisthonotos appeared, thus completing the clinical picture of a classical case of tetanus, subacute in form, predominant on the left. Similarly, the patient observed by Boinet and Monges had received a knife-wound in the left supraspinous fossa. Five days later tetanus set in, with contractures in the left superior member, and these contractures remained localised for a week ; but at the end of this period they invaded the muscles of the neck and face, the right upper limb and the lower limbs remaining unaffected. Lastly, in the case reported by Curtillet and Lombard the malady was once again rather an incomplete tetanus, monoplegic to begin with, then a local tetanus, for the contractures, at first confined to the

wounded upper limb, invaded the muscles of the chest and neck.

The different observations which we are about to reproduce here fall, on the other hand, under the heading of local tetanus, *as in these cases there was never any trace of generalisation.* The cases observed by Pozzi, Routier, Laval, Monod, Carnot and ourselves are peculiarly typical, and enable us to sketch the clinical history of this peculiar local form. We have no intention of bringing together all the published observations of atypical tetanus of the limbs, but only those which appear to us to be particularly interesting, and which will enable us to describe the clinical development of local tetanus of the limbs.

Observation I. (Courtellemont). — Tetanus confined to the left-hand lower limb

C——, sixty years of age, usually enjoyed good health; his antecedents were not in any way remarkable. Towards the end of July, 1909, while working in his garden, he slightly wounded his left foot with the tooth of a rake. He attended to the small wound, which in appearance was insignificant, and in a few days it was healed. On Wednesday, the 11th of August, or about fifteen days after the accident, the left foot became slightly heavy, stiff, and extended at the ankle joint in the position of a talipes equinus; at the same time there was an incomplete trismus. On the next day and up to the 15th August these sensations and this deformation of the foot became more accentuated, without any modification of the trismus.

During the whole of this first period the disorders consisted of a slight trismus and contractures involving the left leg, a trace of the affection in the neck and trunk, and abundant sweats. The trismus never amounted to absolute closing of the jaws; it went no further than making it impossible for the patient to open his mouth completely. It was permanent, and exaggerated by a spasm on the approach

of food. The subject also found it extremely difficult to eat, being unable to masticate.

In the left lower limb there was a permanent contracture, and painful paroxysms were localised in the foot and the leg. The foot was fixed in the position of talipes equinus, the toes were flexed and the contracted calf formed a hard mass. In this condition, intermittent intensifications of the contractures occurred. These paroxysms were very painful; they occurred as the result of a sudden noise (the ringing of a bell, for example), or of movements (when the patient turned in his bed or tried to raise himself). The threat of generalisation showed itself at the moment of these intensified contractures of the left foot and leg; indeed, when the paroxysms were violent the whole body seemed to feel the effect. The trismus increased, the trunk became stiff, and the three remaining limbs also possibly exhibited a slight stiffness, but the patient could not be positive of this last point. On Sunday, the 15th August, Dr Hurtel found the patient lying on his back, incapable of sitting up on account of the stiffness of the trunk, the paroxysms being excited by every attempt to stand up or sit down.

Dr Hurtel diagnosed tetanus, prescribed absolute repose, and darkness, and administered chloral (3 to 8 grammes daily, according to the intensity of the paroxysms). By the evening, and on the following day, the 16th, the condition of the patient had improved, the trismus was attenuated, and all trace of generalisation had disappeared, but the condition of the left leg remained much the same.

We saw the patient on the 17th August. He was in bed, the left lower limb lying abducted, the lower leg half-flexed at the knee; the foot was in hyper-extension—that is, stretched out like a horse's foot—and this attitude appeared to be pushed to the maximum degree; the five toes were strongly flexed. All the muscles of the leg were contractured; they were hard; the relief of the soleus and the twin muscles of the calf was greatly accentuated, the appearance being extremely striking. There was extreme contracture of the muscles of the leg and foot, most marked in the muscles of the calf. This contracture was permanent. It was impossible to modify the attitude of the foot, but the knee could be completely straightened; the hip was mobile, and the thigh could be flexed upon the pelvis, although it

offered a little resistance. Owing to the condition of the foot the patient could not sit down, save on the edge of the bed with the leg pendent. There were no contractures of the muscles of the back or neck, and no trismus.

Sometimes, when the patient made a movement, a painful cramp occurred in the left leg and foot; this was a paroxysm confined to these two regions.

The patient was cheerful, speaking with ease. He presented no sign of visceral lesion.

We administered an epidural injection of 10 c.c of antitetanic serum, and prescribed chloral, in doses of 6 to 8 grammes in the twenty-four hours. The following week went by without aggravation, but without notable improvement, the symptoms remaining entirely confined to the left leg and foot, and there were, rarely, slight paroxysms, also confined to the same regions. During this time the physician in charge of the case administered three subcutaneous injections of 10 c.c. of antitetanic serum.

On the 23rd the dose of chloral was decreased to 3 or 4 grammes; the following night an aggravation of the disorders appeared; numerous and painful cramps of the left leg, a few attacks of cramp in the right leg, some abdominal colics, and some lumbar pains due to spasmodic contracture of the muscles in that region.

On the morning of the 24th the right leg was slightly stiff, and the dose of chloral was immediately increased. In the afternoon the right leg was again normal, but the lower portion of the abdominal wall was rather hard; apart from this sign the disorders were still strictly localised in the left leg and foot. However, the spasmodic intensifications and the cramps were slightly more frequent than on the occasion of our first consultation; we produced them, in particular, by seeking to correct the equinism.

A fresh epidural injection of 10 c.c. of antitetanic serum was administered. From this moment the improvement became progressive; but the patient retained for some six weeks a stiffness of the left foot and leg, and he could not place the foot on the ground without experiencing a painful cramp. Complete recovery was not accomplished until after this long period had elapsed.

Observation II. (S. Pozzi).—**Localised tetanus (early)**

H——, a soldier wounded on the 25th September 1915, near Souchez, by shell-splinters which traversed and splintered the bones of the left-hand tarsal region; the wounded man was given his first dressing on the 25th September, four hours after being wounded, at the advanced dressing station; he received his second dressing on the 28th, or three days after he was wounded, at Aubigny; on the evening of the 29th he reached Broca, where a third dressing was applied (iodoform gauze).

The preventive injection of antitetanic serum (10 c.c.) was administered on the 28th—that is, three days after the patient was wounded. On examination, on the 29th, it was discovered that the two wounds of entry and emergence were exuding a little pus. There was no œdema of the foot. The pain in the region of the wound was not very severe. The general condition appeared to be good. The rectal temperature did not exceed 98·2° F.

On the 30th September a drain was passed through the wound, seton-wise. During the day the pain in the region of the wound increased; then a few convulsive jerks occurred, solely in the left leg, succeeding one another at a few minutes' interval. These jerks were very painful, and attained their maximum when the slightest movement was made.

There was no contracture or cramp in any other part of the body; no trace of trismus. In the evening the temperature reached 100·4° F.

From the 1st to the 4th of October the pain arising from the convulsions increased each day. The jerks occurred with shorter intervals, and became more violent in the left leg and thigh. The temperature rose to 104°.

On the 5th October an extensive opening up of the wounds was effected. The course of the wound was explored, and a few free splinters of bone were withdrawn. On the evening after the operation the temperature rose to 104·7° F.

On the 6th October the temperature dropped a little, but the convulsive jerks became extremely frequent. Every ten seconds the whole of the wounded limb was the seat of the most excruciatingly painful contractions; towards the close of the day a few slight jerks occurred in the right leg.

No spasm existed as yet in the region of the upper limbs; and there was no trace of trismus or contracture of the trunk muscles. This day the second preventive injection of 10 c.c. of antitetanic serum was made.

On the 7th the convulsive jerks increased in frequency and in violence, especially on the wounded side. They continued, though much less violent, on the right side. The patient was screaming with pain, and could be calmed neither by morphia, nor pantopon, nor large doses of chloral.

The evening temperature was 104·9° F.

On the morning of the 8th there was no remission of the jerks. The left-hand lower limb was contractured, the calf being slightly flexed on the thigh and the thigh on the pelvis.

Locally, the cicatrisation of the wounds was not progressing. The suppuration had slightly diminished, but there was no progress toward healing.

The temperature being 103·6 ° F., and the pains atrocious, it was decided that amputation should be performed; the patient insistently demanded it. It was hoped thereby to arrest the nervous symptoms by abolishing their point of departure.

Supramalleolar amputation was performed; no sutures being applied.

Operative Sequelæ.—During the days following the operation the temperature fell, becoming normal on the 10th, or the second day after the operation. The operative wound presented a most favourable appearance.

As for the convulsive jerks, they had diminished neither in frequency nor in violence. On the contrary, the pains were so violent that the wounded man had not a moment's repose; he knelt in his bed, seeking a less painful position. The jerks were as marked on the right side as on the left for two days; then they diminished on the sound side, and finally disappeared entirely. The wounded side was contractured, the limbs being flexed. The pain was more violent when an attempt was made to extend the limb.

No therapeutic agent could overcome the pain. Morphia, large doses of bromide of potassium (8 to 12 grammes daily), pantopon, and extract of valerian were employed, and an application of radium was made without success. Only the bromide and the pantopon gave a little relief. The bromide

was continued for ten days; the pantopon was continued until the end of October.

The jerks and pains then became less violent. But the contracture increased; the flexion of the calf upon the thigh was most pronounced.

There was no trophic trouble in the lower legs.

Following the advice given by Dr Veillon, Director of the Laboratory at the *Clinique Infantile des Enfants Malades*, massive and successive injections of antitetanic serum were administered:

23 October	40 c.c.
24 October	40 ,,
25 October	20 ,,

This active treatment did not appear to produce any marked change. From the 25th October to the 30th the jerks progressively diminished in frequency and violence, and were of rare occurrence, but the contracture was maintained.

Locally, the cicatrisation of the stump proceeded normally. To remedy the persistent contractures subcutaneous injections of perphoxene were tried on the 1st and 2nd of November. The pain caused by the injection rendered it intolerable to the patient, who, however, had at this time already exhibited a remission.

On the 6th November the pains momentarily reappeared in the left limb, with a few jerks. The right limb was thenceforth unaffected. The same day, as a sedative, bibromide of codein was tried, in subcutaneous injection, the dose being 0·02 grammes per injection. The patient appeared to be relieved by this, and was able to sleep better than after the other sedatives.

After the first painful period, the patient passed through a period of permanent contracture without pain. On the 7th December his left lower leg remained flexed at right angles to the thigh, owing to the powerful contracture of the flexora of the knee, the strained tendons of which could be felt by the finger in the popliteal region. There was also a slight contracture of the adductor muscles. Complete extension of the leg was therefore absolutely impossible; moreover, the gastrocnemius was hard and rigid as a lump of wood.

Pressure, unless it was exaggerated, was not painful in the region of this muscle, nor in the region of the thigh muscles. It resulted, from this permanent contracture of the muscles, that the patient was not yet able to benefit by an appliance which would enable him to walk without crutches.

The considerable improvement which has for some days been observed under the influence of massage gives reason to hope that the contracture will presently cease entirely, before the onset of muscular atrophy.

This observation is that of a localised tetanus intermediate between the monoplegic type (predominant) and the paraplegic type, which was established only for a few days, thereupon disappearing without leaving any traces.

Observation III. (Ch. Monod).—Localised tetanus of the right arm

Joseph-Marie Le Br——, thirty years of age, a sergeant in the 8th Battalion of Chasseurs à Pied, wounded, on the 25th September 1915, at Auberive, entered Auxiliary Hospital No. 35 on the 29th September.

First dressing, seventeen hours after the wound; first antitetanic injection, the 27th of September, fifty hours after the wound.

Diagnosis.—Wound caused by a bullet fired from a distance of eight yards. Orifice of entry, small, on the posterior face of the right arm. Enormous wound of emergence occupying almost the whole anterior portion of the forearm. Second orifice a little below the first. The two orifices were drained.

Progress of Malady.—29th September. Temperature, 102·75°-104·4° F.

Moist dressing with Labarraque's solution. Drainage.

1st October.—Temperature, 103·7°-102·2° F. A patch of total gangrene (skin and muscles) extending to the anterior internal face of the forearm, having commenced with an isolated black spot above the wrist. Extensive cleansing with thermocautery was carried as far as the bone, without anywhere finding a sound muscle. On puncture with thermocautery, there was an obvious escape of gases. Moist dressing (Labarraque's solution).

3rd October.—Temperature 101·6°-102·7° F. The gangrene has extended to the hand. Same treatment, serum, electrargol applied. Patient suffering greatly.

4th October.—Temperature, 101·6°-99·1° F. Circular amputation of the upper arm in its middle portion.

5th, 6th, 7th October.—Temperature, 100·4°-101·1°, 99·7°-100·2°, 98·2°-99·1°, F.

8th October.—Patient gets up. Suffers little pain.

9th October.—Shooting pains in the stump, the pains increase during the night. Temperature, 98·2°-98·2° F.

10th October.—Temperature, 97·9°-99·7° F. Very violent jerks in the stump and shoulder, recurring sometimes every three or four minutes, and forcing a cry from the wounded man. These jerks are not clonic but tonic, the member being convulsively drawn toward the trunk. Morphia.

11th October.—Temperature, 100·2°-100·2°. Threads removed prematurely under ether. Carbolic acid, 5 per cent. solution, sprayed over the stump. Chloral, 2 grammes. Antitetanic injection (the first since that given at the outset, fifty hours after the wound). About five hours later the jerks diminished; the patient was greatly relieved. The spraying was discontinued.

12th October.—Temperature, 100·2°-102·6° F.

13th October.—Temperature, 99·7°-103·6° F. The patient still suffering a little; slight contractions.

15th October.—Temperature, 98·9°-100·4° F. At 2 P.M., 3 P.M., and 5.30 P.M., tetaniform paroxysms, with stiffness of the neck and hardening of facial muscles. The hand contracts like a claw, and is slowly drawn towards the right armpit; the head is violently thrown back. The patient loses consciousness. Returns to consciousness at the end of five minutes, but cannot at first speak, and does not understand what is said to him. He is dripping with perspiration. At the end of a quarter of an hour he has fully recovered consciousness, and the slight paroxysms recommence as before.

The patient explains that at the moment of the paroxysm it seemed as though someone seized his arms and forced him to whirl them violently round like the sails of a windmill. Excruciating pain. The same symptoms are exactly reproduced in all three paroxysms. As soon as he comes to himself the patient has no difficulty in opening his mouth

to its full extent and in swallowing. The patient is isolated. Six grammes of chloral.

16*th October.*—Contractures not quite so painful in the wounded arm. Chloral, 8 grammes; subcutaneous injection of 10 c.c. of sulphate of magnesia, according to the formula:

Sulphate of magnesia crystallised with 7 molecules of water of crystallisation .	250 grammes
Distilled water	1000 ,,

During the night the jerks become very painful and force cries from the patient every two or three minutes.

A fresh injection of sulphate of magnesia.

The patient becomes quiet, and sleeps.

17*th October.*—Jerks still painful and very frequent. Eight grammes chloral. Three injections of sulphate of magnesia.

18*th October.*—Same condition. Chloral, 8 grammes. Three injections of sulphate of magnesia.

19*th October.*—Jerks less painful, and sometimes occurring at intervals of several hours only. Chloral, 4 grammes. Two injections of sulphate of magnesia.

20*th October.*—Improvement continues. Six grammes chloral. Two injections of sulphate of magnesia.

21*st October.*—Second antitetanic injection. Six grammes chloral. Two injections of sulphate of magnesia.

Before the injection of serum the patient had two paroxysms at which no one was present. He says he did not lose consciousness, and that the paroxysms were less violent than those of the 15th October, just a week earlier. He was next seen dripping with perspiration, and for a time the pain disappeared. After the injection a fresh crisis at a time when the patient was alone.

22*nd October.*—Two slight paroxysms in the morning. Seven grammes chloral. Three injections of sulphate of magnesia.

23*rd October.*—Greatly exhausted. Suffering greatly. Six grammes chloral. Three injections of sulphate of magnesia.

24*th October.*—Third antetetanic injection. Six grammes chloral. Three injections of sulphate of magnesia.

25*th October.*—Quieter. Fourth antitetanic injection. Six grammes chloral. Three injections of sulphate of magnesia.

26th October.—Fifth antitetanic injection. Six grammes chloral. Three injections of sulphate of magnesia.

27th October.—Sixth antitetanic injection. Four grammes chloral. Three injections of sulphate of magnesia.

In the morning one injection of sulphate of magnesia is given. The patient appearing better, it is decided to stop these injections and to diminish the chloral. But the pains having recurred with great violence towards the evening, with cries at each jerk, two injections are given close together (8 and 8.30 P.M.). The night is quiet.

28th October. — Patient much better. Four grammes chloral. Patient joking. Often goes several hours without jerks. They are slight and not very painful.

2nd November.—Eighth antitetanic injection.

8th November.—The patient no longer has violent jerks, except in the morning, when his bed is approached. If one calls him, even gently, he wakes with a start, uttering a cry. The arm remains painful.

9th November. — Ninth antitetanic injection. Wound almost entirely cicatrised. Temperature oscillates henceforth between 98° and 99·5°.

20th November.—The patient is completely cured.

Observation IV. (Routier).—Abnormal localised tetanus

On the 18th May 1915 a wounded man came under my care for a penetrating wound of the upper and posterior region of the thorax, on the left, with pleural effusion.

Wounded a few days before, he had been given an injection of antitetanic serum.

On his arrival the patient appeared greatly prostrated; there was abundant suppuration, with high temperature. On the following day, the 19th, the countenance was anxious. The patient complained of sharp pains in the left arm, and temperature was 104° F.

This grave condition was not modified on the 20th, but on the 21st the left arm, still the seat of violent pains, was animated by involuntary movements, by incessant clonic contractions.

The forearm flexed itself suddenly upon the upper

arm, while the latter was thrown violently forwards and outwards.

The wrist and fingers remained unaffected. The pain was violent, and the movements continuous, with exacerbations occurring in paroxysms.

Much puzzled to explain these pains and spasmodic movements, I begged my colleague and friend, Babinski, to come and give me his opinion. After a very careful examination Babinski confirmed our apprehensions, affirming that this was indeed a case of abnormal tetanus, and added that its termination would probably be fatal. On the following day, in fact, we observed trismus, pleurothonotos, and then stiffness of the neck.

The pulse quickly became very variable, sometimes being almost normal, and sometimes very rapid, while the respiration assumed a jerky character. At the onset of the accidents we administered a fresh injection of antitetanic serum, and gave the patient, who was isolated, 10 grammes of chloral per diem with morphia at night. This treatment, continued day by day, did not abolish the paroxysms. The patient died of asphyxia on 3rd June.

Observation V. (Routier)

A naval sub-lieutenant was wounded on 25th September in the right scapular region, by a large shell-splinter. Dressed at the Quatre-Vents field hospital, the wound was opened up, and a large hæmatoma evacuated which made, as it were, a fistula in the posterior portion of the upper arm; and two drains were placed in it. An antitetanic injection was said to have been given on the 26th, twenty-four hours after the wound.

The patient was evacuated to Necker, with a large suppurating wound in the right scapular region, but it had a very good aspect, with two orifices near the bottom.

The patient was not suffering, complaining only of the weight of his arm. The general condition was excellent; the temperature on the first evening was 100·4° F, but on the following day it became normal.

Treatment was confined to dressings every second day, moistened with a solution of chloride of magnesium.

He was in such good condition that I authorised his evacuation into the country, but this was not effected.

On the 8th October the patient complained suddenly of a very severe pain in the right thigh. Nothing visible. Temperature, 98·6° F. in the morning; 99·5° F. in the evening.

On the 9th the pain in the right thigh became intolerable. The muscles were slightly contractured; there was marked adductor spasm. Violent headache during the day; slight stiffness of the neck; exaggeration of the reflexes of the whole of the right lower limb with epileptiform spasms. Temperature, 99·7° F. in the morning; 101·3° F. in the evening. Isolation and 10 grammes of chloral ordered.

On the 10th the pains persisted with paroxysmal crises; the stiffness of the back of the neck was more marked. There was also lumbar stiffness. The patient was very nervous; he had photophobia: he complained the moment anyone made the slightest sound or directly one approached him. Morning temperature, 100·4°; evening, 101·3°. The wound seemed to be doing well. Ten grammes of chloral and two subcutaneous injections of a solution of calcium hypophosphate and sodium persulphate.

On the 11th the same signs, with the addition of a slight trismus. Morning temperature, 101·3° F.; evening, 102·2° F. Ten grammes chloral and three injections.

The tongue was dry; the patient drank but little.

This same condition continued, and we pursued the same treatment until the 15th October. The temperature then fell to 99·7° F. The phenomena of contracture and the pains amended; despite this 10 grammes of chloral was given, and the subcutaneous injections were reduced to two, then to one, until the 13th October; the patient still had a few cramps in the back of the neck; finally, on the 22nd, all seemed to become normal once more, and all danger was averted.

The painful phenomena were predominant. There were also contractures chiefly affecting the adductors of the thigh, and a slight trismus and stiffness of the muscles of the back of the neck, but if a very close watch had not been kept these indications might have been unnoticed at the time of their commencement.

Observation VI. (Routier)

M. G——, wounded on the 25th September, entered the hospital at Necker on the 30th. He had a compound fracture of the left elbow, and a wound on the left hip, both being in good condition. Everything seemed as though destined to advance toward recovery when, on the 17th October, the patient exhibited a very painful contracture of the whole of the left lower limb, the thigh being flexed up on the pelvis, the lower leg flexed at the knee-joint; the toes were strongly flexed; all the muscles were rigid. The limb was like wood. The reflexes were exaggerated, with epileptiform twitching. Slight pain in the neck, without stiffness; no trismus; the temperature, which since the 8th October had been normal, rose to 102·6° F.

The patient was isolated. Ten grammes of chloral and two injections of the solution as in the previous case. The same symptoms persisting on the 18th and 19th, I prescribed the addition of an injection of morphia every night.

On the 21st the contracture of the toes appeared to be yielding.

On the 22nd the contracture of the entire limb was no longer continuous.

We observed alternative contraction and flaccidity of the muscles. Vomiting in the night. Parched tongue.

On the 23rd the contracture was greatly diminished. The tongue remained parched; intense thirst.

On the 24th the patient died in the night.

Observation VII. (Routier)

A soldier of the 8th Colonial Regiment was wounded on the 25th September, and entered the Necker hospital on the 15th October. He had two wounds (each with two orifices), one in the upper portion of each thigh, and a slight wound of the perineum, due perhaps to the same projectile, which had not remained in the wounds. When receiving first aid he had been given an antitetanic injection.

Everything appeared sufficiently benign. On the 26th October the patient suddenly complained of pains in the

right knee, which was neither red nor swollen; the lower leg was strongly flexed up at the knee. The patient refused to stretch it out, and cried out when attempting to extend it.

On the 27th the flexion was reduced. The leg was placed on a Bœckel splint. Four grammes salicylate of sodium.

The temperature, which until then had oscillated between 98·6° and 100·4° F., rose to 104° in the morning, and registered 100·2° F. at night. The facial aspect argued in favour of typhoid fever, but the sero-diagnosis was negative.

On the 28th the Bœckel splint was removed, as it could be no longer borne; immediately the leg flexed itself forcibly at the hip and knee joints.

The muscles of the abdominal wall contracted in turn, and during the day contraction of the left arm was noted. On the 29th, 30th, and 31st October all these signs increased; one could no longer approach the patient without his crying out.

Isolation of patient. Ten grammes chloral. Three injections of the solution already mentioned.

Treatment continued until the 5th November, when the chloral was discontinued, the patient showing symptoms of poisoning.

On the following day 6 grammes of chloral was given, per rectum, but it was not retained. The patient was developing a sacral bedsore. Pain still violent, and the contracture of the adductors of the thigh very marked.

During this contracture of the muscles of the leg the foot always remained mobile and supple.

On the 10th November, 6 grammes of chloral was given on account of the greater violence of the pains.

On the 11th the patient could extend his right leg, using his left foot for the purpose, pushing his right foot with it.

On the 13th the chloral and subcutaneous injections were discontinued; they had been continued without interruption from the beginning, to the number of three per diem.

On the 15th the pains and the contracture reappeared. The 6 grammes of chloral and the three subcutaneous injections were resumed.

On the 16th the pains and contractures had ceased. However, the treatment was continued.

The chloral was stopped on the 17th; the injections on the 18th.

The patient is recovering.

Observation VIII. (Routier)

A soldier, thirty-three years of age, wounded at Souchez on the 24th September, entered Hospital 106 on the 1st October, having been given one antitetanic injection.

He had a wound in the head, in the right frontal region, without fractures, numerous wounds of the left upper limb, the shoulder, and the forearm. Many wounds in the two thighs.

A few days after his arrival, pleural effusion on the left side.

16*th November.*—Pleurotomy with costal resection. Enormous evacuation of pus.

17*th November.*—Pains and muscular twitchings of the whole of the left lower limb. Permanent contracture in extension.

Reflexes greatly exaggerated on the left; normal on the right.

18*th November.*—Disappearance of the muscular twitchings.

19*th November.*—Contracture diminished.

The same signs persisted until the 26th.

The contracture no longer appeared save on the occasion of a voluntary movement.

30*th November.*—This day the movements of flexion were still effected slowly, and were preceded by a contracture of all the muscles of the right lower limb, which disappeared when the limb was flexed.

From the commencement of the spasms the patient was isolated and subjected to treatment by chloral, 6 grammes daily, morphia, and subcutaneous injections of Bottu's solution.

All treatment was discontinued on the 26th; the patient had recovered.

Observation IX. (Laval).—Tetanus localised in one leg

André M.——, of the —— Regiment of Infantry, twenty-three years of age, entered the hospital on the 13th April, at

11 A.M. He had been wounded two days earlier, on the 11th, at Les Éparges, by shell-splinters.

Dressed for the first time a quarter of an hour later, on the spot, he received a second dressing at the temporary field hospital at 7 P.M.; and a third on the following day, the 12th, at 4 A.M. Finally, a fourth and last dressing was administered at 2 P.M. at Verdun. There, it was stated, a shell-splinter was extracted from the wound in his chest.

No antitetanic injection.

M——, being examined on the 13th April, presented a wound of the left lower region of the sternum, apparently superficial, and a perforating wound of the left lower leg, the orifice of entry at the juncture of the lower third and the middle third, the orifice of emergence three-fingers'-breadth below the mid-line of the knee-joint.

General anæsthesia by ethyl chloride; the orifices of entrance and emergence of the shell-splinters in the lower leg were enlarged. The wound was cleaned out with hypochlorite solution, 4 per cent.

Moist dressing. Immediately afterwards an injection of 10 c.c. of antitetanic serum was given.

The fever gradually decreasing day by day, and the local condition appearing to improve at the same time, the treatment was confined to the daily cleaning of the wounds with hypochlorite solution until the 19th April.

From this date the clinical picture underwent a transformation. Even on the day before the patient had complained of feeling violent pains in the wounded leg. On the 19th he was examined by X-rays, when a foreign body of some size was discovered in the antero-external region of the lower leg, in its middle third. The two orifices, therefore, did not correspond with the orifices of entry and emergence of one projectile; there was no single perforating wound, but two distinct wounds, one of which still retained the foreign body which had caused it; the other perhaps was a surgical wound.

An hour later, under chloroform, an incision was made in the direction of the anterior tibial artery, five-fingers'-breadth below the wound. Under the superficial aponeurosis, after the separation of the tibialis anticus, fetid gases and yellowish-red pus escaped from the depth of the tissues.

The finger being introduced withdrew a fragment of a shell from the inter-osseous region; this was situated on its anterior aspect. In the depth of the cavity from which this was extracted the forefinger discovered and withdrew a wad of debris from the patient's clothing, the total volume being that of a small nut.

The wound was cleaned with Javal's solution.

Drainage.—The temperature was normal. The question of evacuation was about to be considered, when on the morning of the 23rd there was a fresh surprise: the lower limb was strongly contractured in the region of the foot, which was flexed with the toes in extension. At the same time the wound from which the foreign bodies had been withdrawn was suppurating profusely, and in the neighbourhood of the wound the inflamed lymphatic network could be seen descending toward the thigh.

The patient, interrogated as to the exact period when what he called his "cramps" commenced, admitted to us that he had had them for four days; that they commenced in the foot, and gradually extended to the whole lower leg, but knowing that there was a question of evacuating him he did his utmost to prevent anyone discovering this when dressing his wound.

We immediately administered a fresh injection of anti-tetanic serum, 20 c.c. In addition to this two injections of carbolic acid, 20 c.c. of a 1 per cent. solution were given morning and evening. At the same time we prescribed two doses of chloral per rectum (4 grammes) in the 24 hours.

On the following day, the 24th, the quantity of carbolic acid solution was increased to 80 c.c. per diem, given in two doses, and was continued thus for seven consecutive days, then diminished to 50 c.c. for the four following days. The chloral was continued at the rate of 8 grammes per diem the whole time (11 days).

On the 24th the entire lower limb was in a state of contracture, in forced extension; foot, lower leg, and thigh formed a whole rigid as a bar of iron, which seemed welded to the pelvis.

At the same time the wounded man complained of violent pains in the form of troublesome cramps.

On the 25th the spasm began to diminish; raising the thigh in one hand and pressing the other hand on the lower

leg, one could now cause a slight, very slight flexure of the knee, barely amounting to two or three degrees.

On the 26th the patient suffered less acutely; with a great deal of effort he managed to lift his knee slightly from the plane of the bed, and he himself repeated the very slight flexion produced by us the day before. On the following days the improvement continued. On the 4th May, for example, M—— was flexing the lower leg freely upon the thigh, and with more difficulty the thigh upon the pelvis. As for the foot, it was still forcibly flexed, the toes drawn up by the extensors, whose tendons had the appearance of stretched cords on the dorsum of the foot. Nevertheless, a few slight movements of the toes were seen to occur.

On the 14th May—that is, about a month after the wound—twenty-four days after the first signs of tetanus, the patient had completely recovered from this complication. His wound was advancing favourably toward cicatrisation.

This was a case of monoplegic tetanus which appeared about eight days after the wound, in a man who was not injected until forty-eight hours after the wound.

Observation X. (Laval)

André M——, twenty years of age, was wounded at 1 o'clock in the morning of the 18th October, at Éparges, by a grenade.

Dressed half-an-hour later at the field ambulance; second dressing, with operation, at the M—— hospital, at 11 o'clock.

Antitetanic serum a few hours later.

On arriving in hospital on the morning of the 21st October the presence of two wounds was noted. One, a hand's-breadth in width, occupying the whole of the right-hand thoraco-abdominal region, appeared superficial. The other, in the retro-trochanterian region on the same side, was penetrating; the splinter which caused it was said to have been extracted on the 18th. One could still see the trace of the incision made on the antero-external face of the thigh, about four inches from the orifice of entry.

The treatment consisted of cleaning the thoraco-abdominal wound with hydrogen peroxide, and applying a dressing moistened with Javal's solution, 4 per cent. The wound on the hip, which exhibited no inflammatory reaction, was dressed with the same solution.

The dressing was performed regularly every day, when on the 24th October—that is, six days after the wound—M—— suddenly complained of pain in the right ankle.

Very disturbed night.

27th October.—The pains increased and assumed the form of cramps, which made the patient cry. Morphia was given.

At 2 P.M. the thigh and lower leg were the seat of horribly painful spasmodic contractions. During the spasm the limb would violently extend, as though under the impulse of a stretched spring, and toes, foot, lower leg, and thigh formed a rigid whole. During this tonic convulsion the patient literally roared with pain, this lasting 25 to 30 seconds; then a remission occurred. The limb resumed its normal aspect, but at the end of a few seconds the convulsion reappeared.

These were evidently tetanic convulsions.

Treatment.—1. Antitetanic serum, 20 c.c.

2. Injection of dilute carbolic, 1 in 100, 20 c.c. night and morning.

3. Chloral, per rectum, 3 grammes whenever the patient began once more to complain of the pain.

In consideration of the severity of the case, we

1. Injected 160 c.c. of antitetanic serum, at the rate of 20 c.c. per diem, until the 31st October, except on the 29th and 30th, when we injected 30 c.c. each time.

2. The injections of carbolic acid were increased from 40 c.c. to 80 c.c. daily, and were then decreased to 40 c.c.; they were not discontinued until the 8th November. Very well tolerated.

3. The average amount of chloral given per rectum was 13 grammes in the 24 hours, except for three days, when we were obliged, in order to quiet the patient, to go up to 18 grammes. This medicament was discontinued on the 8th November, simultaneously with the carbolic acid injections.

8th November.—All spasms had ceased; the malady would be regarded as arrested. The spasms had never extended beyond the right lower limb. For three days the pelvic muscles participated in the rigidity, but the latter never mounted higher, nor did it reach the lower limb on the other side.

Observation XI. (Carnot).—Local and late-appearing tetanus

A soldier was wounded in the left arm by a shell-splinter on the 16th June 1915, and evacuated after an injection of 10 c.c. of antitetanic serum.

The wound healed in a fortnight; nevertheless, on the thirtieth day a small blister appeared in the region of the wound, with a drop of pus in it.

From this time the patient felt, at short intervals, slight pains in the wounded arm, but these did not seem to be of any great importance. The patient was therefore allowed out, and then, on the 6th August, sent to his depot. On his return the arm had become painful and its contracture prevented extension; he was exempted from service for a week. Finally, the tetanic phenomena being very plainly defined, he was sent to the hospital for contagious diseases at Épinal, on the 19th August 1915, or more than two months after the initial wound and the preventive antitetanic injection.

On his arrival the patient exhibited a permanent local contracture of the left upper limb, with tetanic spasms. The contracted arm was pressed against the thorax, the forearm flexed and supported by the sound hand.

Occasionally it would be thrown suddenly forward by a painful spasm lasting some seconds. This spasm was repeated several times per minute; it was excited by the slightest sound, or an emotion would cause it.

Although the tetanus was almost entirely localised to the wounded limb, a slight stiffness was observed in the back of the neck, a slight strabismus, and a few rare cramps in the right arm and the legs.

No trismus: no difficulty of deglutition; no dyspnœa; no spasms of the respiratory muscles.

The wound, situated on the anterior face of the upper arm, a few fingers'-breadth from the bend of the elbow, was entirely cicatrised; it appeared neither red nor œdematous, and there was no discharge from it. The temperature was 101·3° F.

Immediately after the patient's arrival an intravenous injection of 40 c c. of antitetanic serum was administered, but as the subject had already been given 10 c.c. of serum two months earlier the possibility of anaphylactic accidents

was feared, and Besredka's method of administering very small initial doses was practised.

On the following day, the 20th August, little modification; the tetanic paroxysms were intense, localised almost wholly in the left arm.

On account of the local character of the contracture (and also of the slightly abnormal strabismus) the nervous condition of the subject was examined, and the cerebro-spinal fluid was drawn off; it was normal. Advantage was taken of the lumbar puncture to administer an intra-rachidian injection of 20 c.c. of serum; there was no anaphylactic reaction. The tetanic cramps, far from diminishing, increased in violence and intensity.

The temperature was 101·6° F.

Two days later it was decided to explore the seat of the old wound, in search of pus or a foreign body which might explain the deposition and late revivescence of tetanic spores.

The incision was made right through the cicatricial tissue, but neither pus nor fragments of clothing were discovered; the only slightly abnormal fact was a discontinuity of the tissues which made it possible to introduce a grooved probe to a depth of 2½ inches, but there was no oozing. Nevertheless, an injection of 10 c.c. of antitetanic serum was made in the region of the wound.

On the other hand, a series of deep injections of serum (30 c.c.) was made along the course of the nerves, on the internal face of the biceps, towards the armpit, or in all an interstitial injection of 40 c.c. of antitetanic serum.

A slight improvement was visible as regards the intensity of the crises, but this was due chiefly to the chloral (6 grammes daily).

The temperature fell, and on the 22nd was only 99·7° F. in the morning, and 100·2° F. at night.

On the 22nd an intravenous injection of 40 c.c. of antitetanic serum was administered.

On the 23rd an intravenous injection of 20 c.c.

The improvement continued, but without accentuation, and the tetanic cramps still persisted, although a little less violent. The chloral was continued.

By this date the patient had in all received, in addition to the 10 c.c. of the preventive injection, and without any

anaphylactic accident, 160 c.c. by intravenous injection, 20 c.c. by intra-rachidian injection, and 40 c.c. by interstitial and paranervous injections.

On the 26th the temperature was tending to rise, and in the morning was 100·4° F. The tetanic contractions appeared to be increasing; there was once more a slight stiffness of the back of the neck, and a few cramps in the opposite arm and the legs. It was decided once again to inject 20 c.c. of serum by intravenous injection, but hardly had the injection been administered when the patient's expression changed; he became congested, and he complained of sensations of heat and general malaise. He felt suffocated, became cyanosed, and was conscious of a sensation of extreme anguish, with difficulty in breathing, and retrosternal pain; at the same time the pulse became thread-like and could not be counted; an extreme fall of blood pressure manifested itself. In short, an intensely dramatic clinical picture was suddenly manifested—precisely that which has been experimentally observed after the "releasing injection" in cases of anaphylactic shock. After a few agonising minutes the purplish face grew ruddy again, and profuse perspiration appeared on the face and limbs, but exclusively on the non-tetanised side. However, during the whole day the patient remained a prey to extreme anxiety. The pulse was 140; the low blood pressure continued, and the situation remained serious.

The tetanic paroxysms had not, however, ceased; they were both frequent and severe; they were still predominantly localised in the left arm, but a few occurred in the legs and the right arm. The dysphagia was so great that the patient could not even swallow fluids. The anaphylactic shock seemed, at this moment, to have accentuated the tetanic phenomena.

On the following day, the 27th August, in the morning, and without any further injection, the patient, who appeared for the time being out of danger, was suddenly attacked by symptoms like those of the previous day. The face became cyanosed; the heart was disordered; dyspnœa suddenly set in, violent and paroxysmal; the anxiety became extreme, with a sensation of imminent death; the pulse could not be counted, the hypotension was considerable, and once again profuse sweats covered the right side, which was not tetanised. Under the influence of injection of ether, caffeine, and

adrenalim solution the blood pressure increased, and the anaphylactic symptoms once more became attenuated.

Nevertheless, the pulse remained low tension and thread-like and rapid (140) the whole of that day. The temperature was 102·2° F. on the evening of the 27th, and 99·8° F. on the morning of the 28th. The anxiety persisted, with psychical excitement. The tetanic cramps were still exacerbated in the left arm; a few occurring even in the legs and the right arm. There was moderate stiffness of the back of the neck. No trismus; dysphagia highly accentuated.

The anaphylactic symptoms continued, with less violence, for some days, characterised by hypotension, tachycardia (140), and extreme malaise.

The temperature remained high: 103·1°, 103·5°.

Locally the wound had become red, œdematous, and indurated, and so, for that matter, had all the regions in which the serum had been injected, but without necrosis (local anaphylaxis).

Then, rather suddenly, from the fourth day onwards, the temperature fell to 102° F. on the evening of the 30th and 99·8°, 99·3° F. on the 31st.

The pulse fell from 140 to 112 per minute. The anxiety was considerably alleviated; confidence returned. The tetanic cramps themselves diminished in intensity and frequency (only 12 in the 24 hours), but there was still, in particular, a permanent plastic contracture of the forearm upon the upper arm.

The dysphagia had disappeared; the patient was drinking, and his appetite was returning.

In short, five days after the anaphylactic shock a true critical period supervened, with rapid amelioration of all the symptoms—not only the anaphylactic symptoms, but the tetanic symptoms also, and with a general return to the normal state.

From this moment the tetanic paroxysms diminished progressively. The permanent contracture persisted for some time longer, with reflex hyper-excitability. The subject remained all day with the left forearm flexed upon the upper arm, the upper arm pressed against the thorax, the sound hand supporting the left arm to avoid positions of extreme contraction.

For hours he remained with a weight suspended to the

affected limb, in order to effect its extension progressively and slowly. There were no further painful cramps. The patient gradually recovered strength. He left, convalescent, on the 15th October, still retaining a slight contracture (in flexion) of the left upper limb, which did not prevent its employment.

Observation XII. (Rauzier and Estor in a thesis by Señor Ramirez).—Montpellier, July, 1915. Late-appearing tetanus localised in the lower limb

L——, twenty-two years of age, was wounded on the 17th January 1915. Slight wound in the right foot, with small fragment of shell enclosed, and a second very superficial wound of the lower leg. The shell-splinter was removed and an injection of serum given immediately after the wound. Intervention in the region of the cicatrix on the foot, after radiography, on account of recent pains and spasms (21st April 1915). No other projectiles.

Since the operation, persistence and recrudescence of the painful contractures in the region of the wounded limb.

This, at the moment of the spasm, became hard as wood along its whole length, and absolutely rigid. On inspection one could see the contracted masses of muscle in prominent relief. The spasms were accompanied by very violent pains, forcing cries from the patient. They were awakened by the slightest touch, an exploration of any kind, or the least excitation of the senses (a noise, etc.). Nothing in the region of the arms, excepting an occasional and transient stiffness of the right arm.

A few contractions of the face were noted, but no trismus, no cervical contracture, and no dyspnœa.

The temperature never exceeded 99·3° F.

The patient was treated with serum, carbolic acid, and large doses of chloral. No respiratory or digestive disorders.

Examination.—Complete rigidity of the lower limbs, above all of the right lower limb, provoking a veritable appearance of ankylosis at moments, and diminishing at intervals.

Nothing in the region of the upper limbs, face, neck, or throat.

The patient could not sit down. General hyperæsthesia was noted on giving injections.

The reflexes appeared to be abolished, and there was no Babinski's sign; the pupils were normal.

The intelligence was maintained, but greatly depressed.

On pressure in the region of the left iliac fossa, a marked feeling of strangulation was noted.

No indications in chest or heart.

Urine normal.

Chloral from the 30th April to the 12th May, at the rate of 10 grammes in the 24 hours.

This was progessively diminished until the 16th May.

Antitetanic injections commenced the 4th May, finished the 14th May.

Injections of carbolic acid commenced the 4th May, discontinued the 19th May. The affected leg gradually became flexed after the 14th, and was finally folded right back; it was only after the lapse of some days that it began to straighten itself again. Stiffness ceased on the 19th May.

Observation XIII. (M. Henri Bouquet)

H—— (Georges), of the 1905 class, discharged for endocarditis on the 8th July 1908, was re-enlisted at his own request on the 8th August 1914. Appointed to the 26th Battalion of Chasseurs à Pied.

Wounded on the 6th September 1914, at noon, during the attack on the Abbaye Wood, near Saint-André (Meuse), where he was acting as a sniper. Remained in this wood with several comrades grievously wounded, like himself, until the 10th September, feeding on blackberries and drinking rain-water caught in the hollows of leaves. He had five wounds: (*a*) an extensive wound caused by a shell-splinter, involving the posterior external portion of the left lower leg with fracture of the fibula; (*b*) a wound caused by a shell-splinter, very deep, in the middle portion of the left thigh; (*c*) a penetrating wound caused by a bullet, in the left forearm; (*d*) a penetrating bullet-wound in the right ankle; (*e*) a penetrating bullet-wound above the left external malleolus. He was also suffering from dysentery.

Picked up by the Germans, on the 10th September, at

6 in the afternoon, and taken by them to the hospital at Saint-André, the first dressings were applied there. Left behind when the enemy retreated, on the evening of the 12th September, he was carried into the French lines on the 13th, owing to the care of a French surgeon, a prisoner like himself. The second dressings were applied on the 14th September, at the Rambluzin field hospital. Taken to the Radepont railway station, and placed in an ambulance train, he reached the Bar-sur-Aube hospital at 10 o'clock at night. There an injection of antitetanic serum was administered the same night.

He was treated at the Bar-sur-Aube hospital from the 15th September to the 18th December. He left it almost cured, one of his wounds still requiring attention, while the dysentery was only ameliorated; he walked with difficulty. For these various reasons he entered Auxiliary Hospital 102, 18 rue Charles-Oivry, Paris, where I attended him.

He told me that six weeks after entering the Bar-sur-Aube hospital he was afflicted by a difficulty in opening the jaws, with acute pains in the region of the temporo-maxillary articulation. A few days later similar pains appeared in the neck, accompanied by a sensation of "stiffening" (this was the word used by the patient himself) in the muscles of that region. When I saw him for the first time these phenomena had diminished in the temporo-maxillary region. The jaws opened almost normally, but when the man spoke the pains recurred for the moment in the region of the jaws. In the back of the neck the pains and contractures were severe and permanent. From time to time there was an exacerbation of these phenomena, and one could then feel the contracture of the muscles under the hand; they became of a woody hardness. When these paroxysms occurred the patient was obliged to lie down, or at least to seat himself in a reclining chair. The pains frequently descended below the shoulders, along the vertebral column. The paroxysms were most frequent during the night and in bed.

At this stage I diagnosed the affection as late tetanus, but considering that these late forms could not possibly be serious, I instituted no further treatment than sedative frictions with alcohol in the regions affected. The phenomena gradually disappeared. When the patient left the hospital, being

temporarily discharged from service, he was suffering only from very slight occasional spasms, which occurred at very long intervals. These ceased entirely a short time after he left the hospital. The dysentery yielded to a treatment, which was principally dietetic, only eight or ten days before he left. At the present time the patient is in good condition, although he still has a certain difficulty in walking and an eversion of the left foot, with a tendency to touch the ground only along its outer edge.

Observation XIV. (M. H. Bouquet).—Late-appearing localised tetanus

Louis R——, of the 1st mixed Regiment of Sharpshooters and Zouaves, entered Auxiliary Hospital No. 102 on the 29th October 1915. Wounded on the 6th October 1915 at Ferme-de-Champagne. Having received the preventive injection of antitetanic serum on the 7th October, he was first under treatment in the hospital at Revigny, before entering our sanitary formation.

The wounds were on a fair way to be healed when, on the 19th December 1915, the wounded man was attacked, at intervals of a few hours, by three tetaniform paroxysms. He was suddenly attacked by violent pains in the epigastric region, the head being slightly retroverted. The face was grimacing; there was, however, no trismus, but if one placed the hand on the abdomen one felt the forcible contracture of the rectus, which was veritably tetanised. The first attack left my diagnosis in abeyance. At the second I suspected delayed tetanus, and administered a subcutaneous injection of 10 c.c. of antitetanic serum. Thereupon, on account of the regulations in force, I was obliged to send my patient to the special department for contagious cases. He was therefore admitted to the hospital in the Lycée Buffon, where we learned recently that the patient had recovered, and that he had been given intravenous injections of antitetanic serum.

Observation XV. (Mériel).—Tetanus localised in the lower limb

Julian L——, of the 342nd Regiment of Infantry, was wounded on the 28th September 1915 at Virginy, by shell-

splinters. The first dressing was applied on the spot, an hour later. The second was applied at the field hospital, where an antitetanic injection was administered.

The patient arrived at Foix (Hospital No. 1) on the 3rd October. He presented a superficial wound of the left frontal region, a perforating wound in the upper third of the left thigh, and another wound of the same nature in the lower third of the left lower leg.

On the 8th October, in the evening, the wounded man began to feel pains in the left lower limb. The wounds had a good appearance. No temperature.

On the 9th October sudden and involuntary contractions were noted in the left lower limb, which were at once exaggerated if the patient was touched. The other limbs were unaffected. No trismus ; no stiffness of the neck. Temperature, 100·8 ° F. ; pulse, 102. An agitated night.

On the 10th, the tetaniform symptoms persisting, with a temperature of 100·4 ° F., an injection of 10 c.c. of antitetanic serum was given.

On the 11th, a fresh injection of antitetanic serum and a dose of 2 grammes of chloral per rectum. The patient was isolated. In the evening the contractions, localised still exclusively in the left leg, returned in paroxysms, which were extremely painful, preventing all sleep, and finally necessitating an injection of morphia.

On the 12th, 13th, 14th, and 15th the condition remained stationary, and an injection of 5 c.c. was repeated daily. The chloral and morphia were also continued.

On the 15th, however, the contractions diminished slightly, but a contracture appeared, particularly accentuated in the muscles of the buttock and the posterior portion of the thigh. The patient also complained of violent pains, and cried out, especially at night. He was accordingly given three doses of chloral per rectum daily, and an injection of morphia about 9 o'clock at night.

During the five following days an attempt was made to discontinue the antitetanic injections, but the contractures and pains became more violent. The injections were therefore resumed on the 21st, and continued daily until the 26th, the dose being 5 c.c. on each occasion.

To break the patient off his daily injection of morphia an attempt was made to replace it by a draught containing

syrup of morphine. None the less he continued to complain all night; he passed urine in the bed; he was delirious, and his appearance was quite abnormal.

The contractions tended progressively to disappear; but the contracture persisted. Between the 28th October and the 2nd November only one injection of 5 c.c. of antitetanic serum was given every second day.

From the 4th to the 19th of November an injection was given only every third day; from the 22nd November to the 3rd December every fourth day; and from the 3rd December to the 17th every fifth day. At the same time the dose of chloral was gradually diminished: from 15 grammes it was reduced to 5 grammes in the 24 hours; first one, and then two doses were suppressed each day; and on the 20th of December the drug was entirely discontinued.

At the same time the dose of morphia was gradually diminished, until it was discontinued on the 25th December.

The tetanic symptoms localised in the left lower limb became slowly attenuated. The lower leg, which had for a long time remained flexed at right angles to the thigh, gradually extended itself, and the contracture disappeared. The toes, at first contracted like talons, gradually assumed their normal position and movements.

The wounds, which had suppurated abundantly while the tetanic paroxysms were still occurring, were now healed.

At the beginning of January the patient was able to get up and walk, still dragging the leg slightly. The general condition was excellent. At the present moment (20th January) he is restored to health.

There was no hysteria in the patient's antecedents. It should be remarked, however, that there was a certain degree of alcoholism, the patient having been carter to a wholesale wine merchant, and accustomed to drinking 5 litres of wine per diem.

Observation XVI. (Personal)

C——, twenty-eight years of age, a second lieutenant, was wounded in Champagne, at Jonchery, on the 25th September, by splinters of a grenade, which occasioned three wounds in the left thigh. He received his first dressing on the same day, about two hours after the wound, at the field ambulance.

A temporary dressing was applied, after the wounds had been disinfected with tincture of iodine.

The same evening the wounded man was evacuated into the Cupperly field hospital, and on the following evening—that is, on the 26th September—about ten o'clock, one of the projectiles was extracted, which was causing violent pain, owing to its superficial position on the internal and posterior region of the thigh, it having traversed the anterior face of the member about the middle portion of Scarpa's triangle.

This projectile was discovered at a depth of about two-fifths of an inch, and, according to the information furnished by the patient, it was about the size of a hazel-nut. The two other wounds were disinfected; one being at the base of Scarpa's triangle, near the outer edge, and about four-fifths of an inch in length, while the other, which was smaller, was on the external face of the thigh, about four-fifths of an inch from the great trochanter.

After the dressing a preventive injection of 10 c.c. of antitetanic serum was given; this was on the day after the wound.

On the 28th September the patient left the hospital at the front and was sent to Paris, where he arrived on the morning of the 29th. He was admitted to Temporary Hospital No. 60.

In this hospital the wounds were dressed daily. A radiographic examination revealed the presence of two large grenade-splinters, about the same size as that which had been extracted, one being situated in the internal and superior portion of the thigh and the other in the superior and external portion.

A little lower the presence of five or six other small splinters was noted. The wounds were suppurating profusely. The pain in the region of the wounds was not very marked. The general condition remained good, and the rectal temperature was normal.

On account of the situation of the projectiles, and also the appearance of muscular contractions, the patient was evacuated, on the 21st October, to the clinic in the Rue Bizet, under the direction of Dr Gosset. There the splinters were localised by means of the Bergonié apparatus, and Dr Gosset thought it best to send the patient to the Hôpital Buffon, on the 23rd October.

At this date the patient stated that ten days after he was wounded, while he was in Temporary Hospital No. 60, muscular contractions appeared on the inner face of the left knee, which were of short duration (two or three seconds) but extremely painful. They recurred about once in two minutes. These contractions increased day by day, progressively, in severity and in frequency, while at the same time they became more painful. There was no contracture or cramp in any other part of the body, no trismus, and the temperature was normal.

About the fifth day—that is, fifteen days after he was wounded—there was a remission for 24 hours, marked by less violent and less frequent pains and contractions, these recurring only about once in five minutes. The wounded man even felt that he was in a fair way toward recovery. But on the following day the convulsive jerks reappeared, more marked than before, and extremely painful. They were then recurring three or four times a minute, and lasted two or three seconds.

The absence of trismus was still noted, and there was no temperature. The patient was able to take his food normally.

Upon his entering our hospital, on the 21st October, the patient appeared to us to be greatly fatigued and anxious. He complained of having had no sleep since the 5th October. On examining him we were immediately struck by the clonic contractions involving the entire musculature of the wounded thigh. At the same time the patient complained of excruciating pains during the paroxysms. The convulsive jerks were recurring three or four times a minute. There were no longer any remissions, and the contractions were localised in the upper portion of the left thigh. No trismus was observed, nor any contractures or pain in the right leg. But the left lower limb was contractured, the lower leg being lightly flexed upon the thigh and the thigh upon the pelvis.

The temperature was not very high: 99·7° F. in the evening.

A subcutaneous injection of 30 c.c. of antitetanic serum was given this day (21st October).

22nd October.—The patient was still in the same condition, complaining of extremely violent pains. He was greatly agitated.

The contractions remained localised in the left thigh.

The temperature, in the morning, was 98·9° F.; in the evening, 99·7° F.

This day a certain constraint was noted in the temporo-maxillary articulation, although there was not as yet, properly speaking, any trismus.

25th October.—The muscular jerks were still very frequent and very painful. At the same time, a fairly well defined trismus was noted in the morning, rendering alimentation difficult. The wounds were suppurating profusely, and, considering the general condition of the patient, the surgeon's intervention was requested; it was hoped that the nervous symptoms might thereby be arrested.

The temperature was still almost normal: 98·9° F. in the morning, and 99·1° F. in the evening.

Dr Berger operated. After making a vertical incision in the Scarpa's triangle of the left thigh, and having penetrated the cribriform fascia, the surgeon removed a foreign body which was situated inside the sheath of the blood-vessels in contact with the femoral vein.

Dr Berger made a second incision in the superior and external portion of the thigh, penetrating the fascia lata, and removed a foreign body.

A third foreign body was quivering behind the blood-vessels, but was deeply buried; the surgeon decided not to attempt its removal.

An injection of 5 c.c. of antitetanic serum was made in each wound, and another of 10 c.c. in the femoral sheath, over the crural nerve.

Dressing.

An injection of 1 centigramme of morphia was given also, and the patient absorbed 20 grammes of chloral.

24th October.—Morning temperature, 100·7° F.; evening temperature, 102·1° F. Pulse, 100.

Milk diet. Injection of 35 c.c. of serum. Chloral, 20 grammes. Morphia, 2 centigrammes.

The local condition was practically the same as the day before. The convulsive jerks were as frequent, as painful, and of the same duration. Trismus worse.

25th October.—Temperature, 100·7°; pulse, 94. Urine, 400 c.c. Subcutaneous injection of 40 c.c. of serum. Chloral, 15 grammes; morphia, 2 centigrammes. Same condition.

26th October.—Temperature, 100°. Pulse, 88. Urine, 600 c.c.

An injection of 60 c.c. of serum. Chloral, 12 grammes.

No perceptible amelioration.

27th October.—Temperature, 100·7°, 102·9° F. Pulse, 120. Urine, 200 c.c.

An injection of 40 c.c. of serum. Chloral, 4 grammes. Morphia, 2 centigrammes.

28th October.—Temperature, 104°, 103·6° F. Pulse, 108. Urine, 700 c.c.

Despite a very marked seric reaction, 10 c.c. of serum was injected. Chloral, 6 grammes. Delirium. The muscular contractions still persisted, frequent and extremely painful. On examination no further localisation of the contractures was observed.

29th October.—Temperature, 100·4°, 100·8° F. Pulse, 100, 120. Urine, 200 c.c. Injection of 30 c.c. of antitetanic serum. Chloral, 8 grammes.

30th October.—Temperature, 100·4°, 101·5°. Pulse, 114. Urine, 2000 c.c.

Injection of 20 c.c. of serum. Chloral, 6 grammes.

31st October.—Temperature, 101·1°, 100·4° F. Pulse, 96. Urine, 1500 c.c. Subcutaneous injection of 10 c.c. of serum; chloral, 6 grammes.

1st November.—Temperature, 100·7°, 100° F. Pulse, 112. Urine, 1700 c.c. Injection of 10 c.c. of serum.

2nd November.—Temperature, 99·3°, 98·9° F. Pulse, 92. Urine, 1500 c.c. General condition improved; but the contractions were still very frequent.

3rd November.—Injection of 10 c.c. of serum.

5th November.—Injection of 10 c.c. of serum. Chloral, 3 grammes.

From this date the contractions diminished in frequency and duration, and a progressive improvement was noted day by day, until on the 12th November the convulsive contractions disappeared.

On the 9th November a further injection of 20 c.c. of serum was given, and on the 11th an injection of 10 c.c.

Recovery seemed complete until the 20th November, on which day the patient exhibited a slight rise of temperature and a slight difficulty in mastication, without any further signs of contracture. On the following day, after an in-

jection of 20 c.c. of serum, all became normal once more, and the patient felt extremely well.

The wounds had cicatrised about six days earlier.

1*st December.*—The patient exhibited merely a functional difficulty in using the left leg. This limb exhibited a persistent stiffness: the movements of the hip-joint were very free, but in the knee, on the other hand, there was an obvious constraint. The movements of flexion were limited. In the tibio-tarsial articulation the derangement was still more marked; the movements of the foot were almost impossible. The leg was in extension. The foot was in external rotation, with a tendency to talipes equinus. There was a very marked retraction of the tendon of Achilles, and a slight muscular atrophy could be noted on the side affected.

Examination of Reflexes.—Percussion of the patellar tendon provoked a tonic contraction of the quadriceps on the affected side.

There was exaggeration of the patellar reflex with clonus of the patella. The Achilles tendon reflex was normal. Babinski's sign was negative. There was no exaggeration of the defensive reflexes, and no indication of spinal lesion.

An examination of the electric reactions revealed a notable diminution of the contractility of the muscles and nerves of the affected limb when stimulated by galvanic and faradaic currents.

In the upper limbs the reflexes were normal. It should be noted that the masseteric reflex was exaggerated.

Here, then, we have a case of early tetanus localised in the left leg.

CHAPTER II

HISTORICAL

Although cases such as those described are excessively rare, it must not, therefore, be supposed that the localised and partial forms of tetanus escaped the attention of the ancients. Hippocrates even, in respect of tetanus, indicated three forms: "straight" tetanus, opisthotonos, and a third more serious form. But Guy de Chauliac, in 1363, was the first to draw the distinction between generalised and localised tetanus.

In 1772 Sauvages described the chronic form of tetanus, which he styled Cathocus, and the lateral form, of which, according to Rose, we find the first indication in Sophocles.

Larrey distinguished acute and chronic, partial and complete tetanus, and recorded examples of localised tetanus.

Dupuytren cited a case of tetanus following upon a contused wound of the thenar eminence; the wound had healed when the patient experienced extremely severe pains with contracture of all the fingers. Similar observations were placed on record by Rémy, Annandale, Gintrac, Gross, and Heinke.

Colles, in 1852, and Follin, in 1861, distinguished between the true general tetanus and tetanoid spasms confined to the injured member.

Legouet recorded the case of a lad of fifteen who was attacked by localised trismus as the result of an accident

which tore off the third phalange of the forefinger, with its flexor tendon.

In 1870 Richelot recorded the case of a wounded man who was affected by a partial tetanus which lasted for several weeks. Having left hospital too soon, the patient was attacked by generalised convulsions, and succumbed in a few days.

In 1883 Bond observed a cephalic tetanus which set in on the twentieth day, and a similar case was recorded by Buisson in 1888, the period of incubation being twenty-two days.

In 1904 appeared Demontmerot's thesis on the paraplegic form, in which four observations were recorded. Esau, in 1910, published the details of a case of local tetanus of the hand. But as we have already remarked, in the majority of these observations the affection described is not, properly speaking, a true partial tetanus. If by this term we understand an infection by Nicolaïer's bacillus, localised in a determined anatomical region, and not proceeding to generalisation, we may say that the history of partial tetanus of the limbs is of recent date. We have seen how the observations of Esau, Boinet and Monges, and Curtillet and Lombard should be regarded; and certain observations which were published by Demontmerot in his thesis should likewise be classified as cases of tetanus with paraplegic onset rather than as observations of paraplegic and partial tetanus, for after a transient and initial localisation of the contractures in the lower limbs, trismus appeared, with stiffness of the neck and trunk.

We may therefore consider, in accordance with the definition which we have given of local tetanus—"an affection which is local during its entire development"

—that observations of local tetanus of the limbs, at all events of the monoplegic form, have not long been known.

In May, 1915, appeared the first report of a case of local tetanus of one leg, in a work of Courtellemont's.

Then, in June, 1915, Albert Ramirez Martinez reproduced in his thesis a very instructive observation by Professors Rauzier and Estor. This was of a late-appearing localised tetanus, the seat of which was one of the lower limbs.

Then Pozzi, from the tribune of the Academy of Medicine, in November, 1915, described a typical example of early local tetanus of the limbs. The localisation was in the first place monoplegic, then, temporarily, paraplegic, but with a marked predominance in the wounded leg. It persisted for five weeks, and was followed by recovery.

This observation, the first of this rare clinical type, evoked, by its interest, the publications of Monod, Routier, Laval, Carnot, Courtois-Suffit and René Giroux, and Mériel. Now that these cases are better known, they have become less rare. At the present time numerous cases have been recorded, and Dr Fricker, in connection with a certain number of personal observations, has lately reviewed the question of the partial forms of tetanus in his inaugural thesis.[1]

In the following pages we shall describe the peculiar symptoms and the special evolution of this local and atypical form of the tetanus.

[1] Unfortunately we have not been able to consult this thesis; we feel, however, under an obligation to mention it, in order that the reader may consult the observations recorded by this writer.

CHAPTER III

MONOPLEGIC FORM

1. Period of Incubation.—The period of incubation is the interval of time which elapses between the moment of infection and the moment at which the first tetanic symptoms appear. Generally speaking, inoculation with the bacillus gives rise to no immediate sign. No local or general phenomena reveal the multiplication of Nicolaïer's bacilli, nor the progressive invasion of the system by the toxin.

Here we have an *insidious phase*, during which the tetanic infection is developing, although nothing enables us to detect it.

This insidious phase is of very variable duration. It may be brief or prolonged, so that there are two distinct forms of tetanus, distinct, at least, as far as the appearance of the first tetanic manifestations is concerned. These are:

1. Early or precocious local tetanus.
2. Late-appearing local tetanus.

In the first variety the incubation period is in general of brief duration, the first symptoms usually appearing between the fifth and tenth day. This was the case with the observations recorded by Pozzi (fifth day), Laval (eighth and ninth days), and ourselves (tenth day). In this connection, whenever the first signs of tetanus appear during the fortnight following the wound, we regard the disease as being of the early or precocious form.

In the second variety, the late-appearing form of localised tetanus, the period of incubation is always lengthy, sometimes extremely lengthy. This, by the way, is one of the most important characteristics of this form.

Generally speaking, the first clinical indications of the late form of local tetanus appear from twenty to thirty days after the wound, when the latter is becoming cicatrised, or is already completely cicatrised. Sometimes this lapse of time is even greater.

Demontmerot has recorded a case in which the first symptoms did not appear until six weeks after the infliction of the wound. In Rauzier and Estor's case the period of incubation was three months. Finally, it must be mentioned that Huntington has cited a case in which tetanus appeared seven months after the wound, the latter being still discharging. This long incubation in the late-appearing form is often, however, apparent only. Bérard and Lumière have, in fact, demonstrated that this variety often develops as the result of a surgical traumatism, appearing six, eight, ten, or fifteen days after operative intervention, which usually takes the form of a tardy cleaning out, the search for a foreign body, or a secondary amputation, sometimes—indeed, as a rule—involving the region of the wound, and sometimes a region remote from the wound. It seems logical to accept the period which elapses between the surgical traumatism and the appearance of the first signs of confirmed tetanus as constituting the actual period of incubation. The spores have hitherto remained in a condition of latent vitality, enclosed in a crevice which isolates them for the time being, or encysted in a shell of inflammatory tissue. By an exploration or surgical operation of some sort these spores are set free, sowing

themselves in the adjacent tissues and secreting their toxins there. These, therefore, are cases of secondary reinfection, due to tardy surgical intervention.

The development of these late-appearing forms of tetanus permits us to refer them to latent microbic infection due to the mechanical liberation of the spores, analogous to that of postponed infection. This has been demonstrated experimentally by Tarozzi, Canfora, and Vincent, who, after injecting cultures of Nicolaïer's bacillus into the veins, or even under the skin, have found spores in the viscera of the animals experimented upon several weeks after injection. They have shown that a traumatism, or any factor which diminishes the resistance of the organism, as cold, for example, may result in an outbreak of delayed infection.

On other occasions the surgical traumatism does not give rise to tetanus, but accelerates the development of tetanus in incubation. Thus in the cases recorded by Vallette and Leriche tetanus made its appearance thirty-seven and forty-two days after the wound, and only twenty-four to forty-eight hours after operation. This lapse of time is too short to be regarded as a period of incubation.

From these considerations it results that it is often difficult to form an approximate estimate of the period of incubation in the late-appearing forms, but it always exceeds twenty days. This period of at least twenty days should indeed be regarded as the minimum incubation period in the late-appearing forms of localised tetanus.

2. Period of Onset.—Whether the form in question is early or late-appearing, the earliest symptoms are assuredly those which it is most important to under-

stand, for it is a matter of urgency that an early diagnosis should be established, in order that tetanus patients may be treated from the commencement of the infection.

The first symptoms are often unnoticed if one is not careful to interrogate and examine the patient with the greatest care. If the patient does not complain of them these first indications may be regarded as unimportant by a physician who is not on the watch for them, so that it is important to insist upon the first manifestations of the onset of localised tetanus.

Prodromal signs of a local or general character may be noted.

Local Signs.—In the region of the wound, which may be superficial—this, according to some writers, explaining the benign character of certain cases—we may note an arrest of fleshy vegetation, or of suppuration, or swelling, with redness of the skin and mortification.

More significant, and more constant, are shooting pains in the region of the wound, and spasms in the neighbouring muscles, followed by cramps and jerks or twitchings.

But we must at once observe that such local prodromal phenomena as spasms are exceptional in the late form of localised tetanus, which usually declares itself at a period when the wound is cicatrised, so that it might be described as *cicatricial tetanus.*

The pains most commonly appear in the affected limb, but this is not invariably the case ; thus to cite a typical example, in the case recorded in Observation V. the wound was situated in the right-hand posterior scapular region, while the pains and contractures first appeared in the right-hand lower limb.

The patient experiences a slight sensation of contrac-

tion in the affected limb, and pain, presently followed by a sudden and involuntary contraction of certain muscles.

A *sudden pain, localised* in one limb, *without apparent cause*, is an important indication in a wounded man, and the occurrence of pain should always arouse attention and suggest the possibility of a tetanic outbreak.

The pain in question may be fugitive, giving rise to a sudden movement, or a rheumatismal pain, or there may be stiffness in the wounded limb. In addition to pains in the region of the wound, a slight feeling of fatigue in the jaws is sometimes observed.

This pain is presently followed by contracture in the same region. It must be remembered that local cramps occasionally precede trismus even in the normal and generalised forms of tetanus ; so that in order to establish an early diagnosis the physician should never await the appearance of trismus, which in the localised forms is always transient.

Foreign writers have also insisted upon the occurrence of cramps at the outset in their recent dissertations (1914-1915) upon tetanus.

The essential characteristic of the cramps is that they are caused more particularly by external excitation. A cry uttered in the room, the sudden closing or opening of a door, the sudden switching on of the electric light, the fall of any object, the noisy tread of an orderly, the touch of cold hands—all these incidents may provoke the appearance of cramp.

When the patient himself complains that these contractures result from external excitation, there is no further room for doubt : the patient is certainly suffering from tetanus.

The cramps often attack certain groups of muscles,

and confine themselves to these during the whole course of the malady; or they may spread over the whole of a limb. The contracture is total or partial, and in this latter case one segment of the limb may escape it. This was the case in two of the observations published by Routier: the hand, in the case of one of his patients, remained free, with a contractured upper arm and forearm; in the other case the lower leg and thigh were rigid, but the foot remained mobile. In the case observed by the present writers the contractures were strictly localised in the left thigh. It must also be remembered that the initial seat of the contractures, or of the symptomatic pains, may be far removed from the point of inoculation. In certain cases, which are, however, rare, the contracture may occur in the muscles of the jaw, but this symptom is always slight and ephemeral. It amounts merely to a certain difficulty in opening the mouth; the patient can eat, drink, and speak normally.

It must also be remembered that at the very beginning the patient may exhibit *merely a slight stiffness*, which does not prevent his walking. In certain cases the physician himself discovers this stiffness on the occasion of an examination or a dressing.

As Montais remarks, this slight stiffness may be brought to light by attempts to reduce it, by voluntary movements, or by any local excitation. Palpation reveals, in such cases, hypertonia of the muscles which contract through their whole extent when subjected to any excitation. The muscular contraction thus provoked is normally extensive and prolonged, and perceptible to the patient; after the lapse of a few days it is only too evident.

The general symptoms, in a case of local tetanus, do

not attract the attention of the clinician, and, above all, are less significant than the pains and cramps.

The general prodromal symptoms are headache, anorexia, yawning, lumbar pains, peculiar sensitiveness to cold, a tendency to perspire, disturbed sleep, dysuria, and constipation.

The rise of temperature is very irregular. This fact has been noted by all those writers who have latterly treated the subject. Sometimes there is a rise of temperature at the outset; sometimes it occurs only after the lapse of two or three days, and we shall see that although the fever sometimes attains 104° F.; it is more usual to see the thermometer mark 100·5° to 101·5° F., so that the examination of the temperature does not as a rule furnish information of any value.

The pulse is fairly normal.

On the other hand, the change of expression observed in the patient is an indication which demands our attention. When describing the attenuated and slowly developing forms of tetanus we shall see that Claude and Lhermitte have laid great stress upon the facial aspect of the patient.

In the localised forms one is struck by the expression of anxiety of the countenance during the whole development of the disease; an anxiety which is increased by the dread of sounds and movements, and which disappears the very moment the pains and contractures cease.

Lastly, we shall call attention to the fact that from the very commencement of local tetanus there is observed, in the limb which is the seat of the pains and contractures, a certain nervous irritability which is revealed by an exaggeration of the reflexes, which becomes manifest as the acute phase approaches.

To sum up. The mode of onset of local tetanus of the limbs is almost always identical. Although there is no appreciable cause, although neither the situation nor the nature of the wound give rise to suspicion, a pain suddenly occurs in one limb, usually the limb neighbouring upon or containing the wound, and then contractures make their appearance, recurring under the stimulus of external excitation. The temperature is not very high, but the patient's facial expression becomes anxious. It is as though he were aware that the tetanus was developing toward an acute stage.

3. Period of Acme.—During the period of acme the signs already described—namely, the pains and contractures—attain their maximum intensity; and it is during this period that the tetanic infection almost invariably exhibits, in the localised forms, ephemeral phenomena of generalisation. These phenomena, however, cancel none of the characteristics peculiar to the special localisation of the disease. A local disease, it remains local, despite transient trismus, and a trace of stiffness in the neck, despite the respiratory troubles which occur in certain cases.

These localised contractures are the signs which dominate the clinical picture: contractures which are sometimes accompanied by extremely violent pains, which force the patient to cry aloud. They are sometimes slight and tardy, but in the majority of cases they are severe and appear early, constituting a significant indication.

The pains coincide with the spasms. Sometimes they radiate through the whole of the wounded limb, sometimes they remain localised in one segment of the limb. Sometimes they extend even further, invading other

regions : the opposite limb, the other limb on the same side, the abdomen, etc. ; or they may be confined to a determined region. Their essential characteristic is that their severity is intensified by the stimulus of the slightest sound, or a sudden movement in the neighbourhood of the patient's bed.

The *contractures* are intense ; they may, like the pains, become generalised throughout the entire limb, or they may be confined to a single segment ; often enough they ascend as far as the abdominal wall. They may also sometimes invade, in a secondary and ephemeral fashion, the opposite limb, or the other limb on the same side. They may constitute the only symptoms of partial tetanus, and in any case they constitute its primary element. They may be divided into two individual types.

They may consist of extremely painful convulsive jerks, which are characterised by clonic movements. These usually occur in paroxysms, which, infrequent or only of moderate frequency at first, become more and more frequent as the malady develops. In our own observation, for example, the clonic contractions in the thigh recurred three or four times per minute ; in the case observed by Pozzi the whole of the wounded leg was every ten seconds the seat of painful contractions of the most afflicting character, until finally the convulsive jerks no longer exhibited any remission, so that the wounded limb remained wholly contractured, the lower leg being slightly flexed upon the thigh and the thigh upon the pelvis.

In other cases (of which examples are recorded in an observation of Routier's, and one of Laval's) these convulsive jerks are not observed, but contractures appear which are persistent from the outset, so that the

limb, on palpation, feels like a *block of wood.* As a rule there is an excessively painful contracture of an entire limb ; in a case of Routier's the thigh was flexed upon the pelvis, and the lower leg upon the thigh ; the toes were strongly flexed, and all the muscles were rigid. In Laval's case the contracture, which commenced in the foot, gradually gaining the lower leg, had by the following day invaded the whole limb, which, as a result of the generalised contracture, was in a position of forced extension : the foot, the lower leg, and thigh formed a whole, rigid as a *bar of iron,* which seemed welded to the pelvis.

We see, then, that the contractures may reveal themselves, clinically, by clonic movements recurring in paroxysms of varying frequency, or by a generalised tonic contracture, which gives the limb a very characteristic appearance. Contracture in extension, the usual type of contractures of the lower limb, is the rule ; contracture in flexion is a rarer type.

We have mentioned that it is during this period of acme that the traces of generalisation may make their appearance, enabling us with certainty to establish a diagnosis of tetanus. It must not be forgotten—and we wish to lay stress upon this point—that these signs are ephemeral, are not very marked, and are sometimes absent.

In some cases the patient complains of a pain situated in front of the ears, with difficult and painful movements of deglutition. This phenomenon, which in the classic forms of tetanus usually marks the commencement of the period of acme, is here of secondary importance, and as a rule disappears within twenty-four or twenty-eight hours. The pain, moreover, is quite moderate.

Stiffness of the back of the neck is more frequent; the transient contracture is not very marked. The forward flexion of the head and neck is painful for a few days, at the time when the localised tetanic contractures of the wounded limb reach their maximum. The contracture is never accompanied by the retroversion of the head.

The muscles of the face are in general little affected, and the *risus sardonicus* is never observed.

The muscles of the trunk are usually unaffected; opisthotonos, emprosthotonos, and pleurothotonos are never observed.

Routier, on the other hand, has mentioned, as an important symptom in localised tetanus, *a more or less marked contracture of the muscles of the abdominal wall.* We must not attach to this sign the importance attributed to it by Berard and Lumière, in respect to the gravity of the prognosis. These writers regard it as the precursor of contracture of the respiratory muscles and asphyxia; but in many cases in which this abdominal contracture has occurred recovery has followed.

General Indications.—General indications have not the same value here as in the classical form of tetanus. For example, the *rise of temperature* is very irregular. Sometimes it rises at the outset, sometimes only two or three days later, and while it sometimes attains 104° F., it is more usual to see the thermometer oscillate between 100·5° and 101·5° F. However, the thermal curve is usually ascendant from the commencement of the pains, remaining high until their disappearance.

In the usual form of tetanus the temperature is a great help to prognosis; if the temperature is very high the case is very serious; if the temperature is moderate

the tetanus will be a chronic, less serious form, from which recovery is possible. In localised tetanus the indication derived from an examination of the temperature is no longer of value. Thus in the two fatal cases recorded by Routier the temperature never rose above 102·2° F.

The pulse is accelerated, but remains regular. The rate varies, as a rule, from 100 to 120 per minute, but one never observes the extreme rapidity, nor the feebleness, nor the irregularities which are noted in the normal forms of generalised tetanus.

We may add, also, that the urine diminishes in quantity, that retention of urine may occur, and that the face becomes covered with sweat at the moment of the convulsive paroxysms.

The facial aspect of the patient, on which we insisted when speaking of the period of onset, becomes still more characteristic. The patient is extremely anxious, even during the periods of calm, and his face assumes a curious expression, which strikes the observer at the first examination. We shall see that this peculiar facial aspect is plainly defined in the attenuated forms of the disease.

The pulmonary disorders are not very marked, the acceleration of the respiratory movements is slight, and, although in the ordinary form of tetanus the contrary is the case, the respiration never becomes dyspnœic ; it is never more than slightly embarrassed.

Let us note that the patient, as in the generalised forms of the tetanic infection, always exhibits photophobia and a terror of noise and movement, which are due to the hypersensitiveness of the organs of the senses. Lastly, the intelligence, even in the midst of the painful paroxysms, always remains unaffected.

Examination of Reflexes.—Examination of the reflexes in local tetanus reveals a constant exaggeration of the osseous and tendinous reflexes, with ankle and patellar clonus. Percussion of the zygoma causes, in certain patients, a sudden extensor movement of the head. The masseteric reflex may be exaggerated; it was so in the case observed by the present writer.

This exaltation of the osseous and tendinous reflexes is associated with a hyper-excitability of the muscles and nerves to galvanism and faradaism. This sign is observed also in the attenuated forms of tetanus described by Claude and Lhermitte. It must be remembered, however, that the exaggeration of the reflexes may be accompanied, as in the case observed by the present writers, with hypo-excitability of the nerves to electric stimulation.

In localised tetanus, as in the generalised form, the blood exhibits no special reaction. The hæmatological formula depends upon the condition of the initial wound and the presence or absence of septicæmia or anæmia.

It is the same with the cerebro-spinal fluid, which reveals no appreciable modification; there is no cellular reaction, no increase of albumin. The liquid yielded by a lumbar puncture is sterile and non-toxic.

To sum up. The period of acme in local tetanus, whether early or postponed, is characterised by:

1. Contractures confined to one limb, with more or less frequent spasmodic paroxysms, without lasting phenomena of generalisation.

2. No very noticeable general signs; the temperature is not high; the pulse is regular, not exceeding 120, and the respiration is but slightly embarrassed.

3. An exaggeration of the reflexes.

4. A chronic development and a tendency toward recovery in the majority of cases, as we shall presently see when considering the progress and the prognosis of the various forms of local tetanus of the limbs.

Diagnosis

Positive Diagnosis.—While the diagnosis of generalised tetanus presents no difficulty; while trismus, opisthotonos, and the clonic contractions of the whole body form a symptom complex easily recognised, matters are otherwise in the partial forms of tetanus, at all events in the beginning. We must suspect a localisation of tetanus when, the wound being still uncicatrised, or well on the way to cicatrisation, the wounded limb sooner or later becomes the seat of pains or cramps which must be regarded as the first manifestations of contractures. Above all, the diagnosis must incline toward the tetanic infection when the pains and contractures are influenced, awakened, and intensified by sounds or movements or lights. In such a case one may affirm with practical certainty, even if the patient received a preventive injection of 10 c.c. of antitetanic serum within a few hours of being wounded, that he is suffering from tetanus.

Nevertheless, it must not be supposed that hesitation is impossible; on the appearance of the first contractures it is often difficult to form a decision, for which reason we would gladly appeal to the laboratory for the certain information which clinical science is unable to yield. Unfortunately, as we shall see, there is no sero-diagnosis of tetanus by the agglutination test (Courmont). Proceeding from this fact, certain writers have recommended a direct search for the

presence of Nicolaïer's bacillus in the wound. But the bacteriological examination of the secretions of a wound often yielding results of too uncertain a nature, many clinicians are of opinion that experiments upon animals are greatly superior to morphological examination, or culture, for the purpose of determining whether the tetanic bacillus does or does not exist in the wound. Jacobsthal even writes that this is the ideal method, although such experiments occasionally fail. This failure may be attributed to the degeneration of anærobic germs resulting from a mixed infection.

In the early stage of tetanus, accordingly, the laboratory is of no value as an auxiliary to clinical science, and it is greatly to be regretted, from the therapeutic point of view, that the presence of the toxin in the patient's blood cannot be determined before the first symptoms make their appearance.

M'Clintock and Hutchinson, however, were able to prove the presence of the toxin in the blood of sheep which had been infected with tetanus four days before the appearance of the clinical indications.

Differential Diagnosis.—Under these conditions it will be understood that right at the outset, particularly in the late-appearing localised forms, a certain number of affections may give rise to confusion, more or less faithfully simulating partial tetanus.

1. *A spasmodic monoplegia of cerebral or medullary origin* may be characterised by cerebral disorders (ictus, dysarthria, vertigo, headache, sphincterial trouble, and modifications of the tendinous reflexes). There is no trismus, and no painful and spasmodic intensification of the phenomena, and the development is not rapid. It is easy to differentiate tetanic paroxysms from the paroxysms of Jacksonian epilepsy, and from

the syndrome described by Kojejnikov, under the name of continuous partial epilepsy.

2. The same is true of *incomplete hemiplegia* with predominance of the signs in one limb.

3. The syndrome of *excitation or irritation of the motor nerves and the mixed nerves*, which may reveal itself, apart from the pains, by the exaggeration of the tendinous reflexes and by contracture, is more difficult to distinguish from partial tetanus. The examples recorded by Le Fort, Dupré, Schœffer, and Le Fur are particularly instructive in this connection.

René Le Fort, in a work entitled *Pseudo-Tetanic Symptoms in Wounded Men suffering from Lesions of the Nerves complicated by the Presence of Foreign Bodies*, refers to the clinical history of three patients, who, having been previously given a preventive injection of antitetanic serum, exhibited painful and spasmodic symptoms in the wounded limb, with contracture in hyper-extension in one case, and in hyperflexion in the other two cases. These symptoms disappeared after the removal of foreign bodies which were in contact with the nerves. The hypothesis of partial tetanus cannot be rejected with certainty, at all events in one of these cases, for the contracture invaded the unwounded limb, and the symptoms at one time assumed a serious character which was not consistent with a simple nervous lesion.

The observation published by Dupré, Schœffer, and Le Fur dealt with a patient wounded on the 20th September 1914, who had not received a preventive injection, and who was attacked, a week after the traumatism, by a serious and acute form of tetanus, which terminated in recovery. The right leg remained flexed, and an operation was performed on the sciatic

nerve on the 7th January 1915. In June the limb still presented tetanic spasms, occurring, in particular, on walking, and remaining refractory to all treatment. Dupré, Schœffer, and Le Fur discuss the possibility of a psycho-neurosis, or of a chronic tetanus. While the hypothesis of a psycho-neurosis is hardly probable, that of tetanus is more so; but we may ask ourselves whether the lesion of the sciatic nerve was not the origin of the tetanic spasms. However, the existence of a previous attack of acute tetanus, and the character of the spasms, which were not localised in the wounded limb, but were generalised, sometimes invading the masseters, argue in favour of chronic tetanus. It may also be the case that the lesion of the sciatic nerve favoured the persistence of the spasms after the development of acute tetanus, and determined their predominance in the wounded limb. This is a complex problem, and one difficult of solution. A nervous lesion may not only simulate a local form of tetanus, but may also favour its development. It will be understood, in short, that a slight wound of a nerve might localise the action of the tetanic toxin along its course, but we may also conceive that a nervous lesion anterior to tetanus might favour the appearance of the latter. The observation published by Phelip and Policard shows this determining influence; it deals with a subacute and benign case of tetanus, which, in spite of two preventive injections, developed seventeen days after an excoriation of the hand; the wounded limb, which was the initial seat of the tetanic signs, had several years previously been attacked by a traumatic neuritis of the median nerve.

4. The contractures or pseudo-contractures following upon lesions of the bones, the joints, the tendons, or

the muscles, are differentiated by their stability and the fixed position imposed upon the limb, while a careful examination of the region involved will always enable the physician quickly to discover the cause of the contractures.

5. *In tetany* we find contractures of the muscles of the extremities, which may extend to the limbs, occurring in paroxysms of very variable duration. The onset may occur unheralded, or may be preceded by prodromal symptoms consisting of disorders of sensibility, formication, numbness of the hands and fingers, and muscular stiffness, and of general disorders: general malaise, cephalalgia, and fever. The contracture is the capital sign of tetany.

The contractures involve, simultaneously or alternately, the upper and lower extremities; they are sometimes confined to one pair of extremities only, usually the upper. The contractured muscles are hard, and raise the skin like tightly stretched cords. It is usually fairly easy to reduce the contracture and restore the members to their normal attitude, but the deformation reappears directly they are released.

The pains, which are spontaneous and moderate, occur in the affected muscles, and along the nerves of the limb, sometimes irradiating over the trunk.

These contractures, as we have remarked, occur in paroxysms lasting five, ten, or fifteen minutes, occasionally one, two, or three hours. The reappearance of the sensation of formication announces the termination of the paroxysms. After a period of repose the fit recurs, and the series of fits constitutes the attack, which may last for some days, or may persist even for one, two, or three months.

Three forms of tetany may be distinguished: a benign form, a form of medium severity, and a grave form. It is more particularly the benign form, in which the contracture may involve a single member, which may be confounded with localised tetanus on a superficial examination.

Examination of the mechanical and electrical excitability of the muscles reveals the existence of several signs which are almost pathognomic. These are Trousseau's sign, Weiss's sign, and Chvostek's sign, or the sign of the facial nerve.

Trousseau's Sign.—At any time before the termination of the malady one may cause the fits to recur at will, even though none have occurred for one, two, or three days, or more. This is effected, says Trousseau, by exerting compression on the affected member, either upon the course of the principal nerves, or upon the blood-vessels. Thus, by exerting pressure on the median nerve of the arm, or the brachial plexus above the clavicle, the contracture occurs immediately. In the lower limb, if the femoral artery or the sciatic nerve be compressed, or a ligature applied to the thigh, the muscular spasms recur in the lower extremities, although less readily.

Weiss's Sign.—The percussion of the temporo-facial branch at the outer angle of the orbit may provoke a contraction of the orbital, frontal, and superciliary muscles.

Chvostek's Sign, or the sign of the facial nerve, reveals neuro-muscular hyper-excitability of the face. Slight percussion of the facial nerve in the cheek causes a

sudden contraction, "like a flash of lightning," of the muscles innervated by the facial nerve.

Another sign has been described, which is obtained by raising and forcibly flexing the lower limbs, maintained in extension, upon the trunk; a prompt contraction of the muscles of the legs is produced, placing the foot in forced inversion.

In tetany we find also hyper-excitability of the muscles and nerves to galvanism. The reflexes are maintained, and often exalted, and one occasionally notes vasomotor and trophic disorders. In addition to these signs there is, lastly, a special etiology which determines the diagnosis. It is at present supposed that tetany is caused by an intoxication which acts upon certain elements of the nervous system, and is itself caused by digestive troubles or by a special glandular insufficiency (the parathyroid theory). Recent investigations, indeed, permit us to suspect, in cases of tetany of gastric origin, a parathyroidal insufficiency, and the toxic disorders resulting therefrom. We know, since the publication of the results of Gley's investigations, that ablation of the parathyroids sometimes gives rise in man and in certain animals to grave tetanic symptoms which are often fatal (the tetany of operative myxœdema).

6. *Acute strychnine poisoning* might possibly cause confusion. It greatly resembles tetanus, especially at the outset, for at this period the contractures caused by strychnine affect only the muscles of the lower limbs, becoming generalised subsequently.

The intoxication is preceded by yawning and retinal hyperæsthesia. The pupils are dilated, and objects appear green to the eye. There is often delirium from

the outset, while in tetanus the intelligence is usually unaffected.

7. *Hysterical contractures* may also simulate tetanic contractures, the more so as they may be partial, occupying a group of muscles, a segment of a limb, or a whole limb.

The contracture appears after a convulsive attack, or more rarely without appreciable cause, when it may be the first manifestation of neurosis (Babinski).

Its onset is sudden and rapid, and it attains its maximum intensity at once, or very quickly. The rigidity may be extreme, and very difficult to overcome, causing excessive deformation. Hysterical contractures are usually accompanied by objective disorders of the sensibility : anæsthesia, or hyperæsthesia, whose topography is regional, often being confined to the territory occupied by the contracture.

Its duration is extremely variable. It may persist for a few days or a few months. It may disappear as it came—that is, suddenly, after an attack, or as a result of suggestive treatment.

It may also disappear slowly, little by little. It ceases temporarily, and sometimes finally, under chloroform. Its differential diagnosis is readily established by the fact that the reflexes are not modified (Babinski); there are no spasmodic and painful intensifications, and there is no trismus.

Everything being considered, the establishment of the diagnosis of localised tetanus is, at the outset, a very delicate matter, but the affections which may cause confusion, in particular tetany, the syndrome of excitation of the motor nerves, hysterical contractures, and acute strychnine poisoning, possess a sufficiency of peculiar and characteristic signs to make it possible,

in the majority of cases, to diagnose them promptly. Moreover, the evolution of the disease furnishes data which assist us to recognise the nature of the contractures, and to show that we have to deal with a localised tetanic infection.

CHAPTER IV

PARAPLEGIC FORM

This form of the tetanic infection, localising itself in two symmetrical members, was particularly considered by Demontmerot in his inaugural thesis in 1904. But certain of the cases recorded by this writer do not come under the heading of partial tetanus, for after a first ephemeral localisation in the two lower limbs trismus and stiffness of the neck and the trunk set in. These were therefore cases of classic tetanus with paraplegic onset.

It must be remembered, also, that hybrid forms may occur, intermediate between the monoplegic and paraplegic types. The one type shows itself for a few days only, disappearing and leaving no traces. Pozzi's observation is the first published record of this clinical variety. It describes a localised tetanus with the monoplegic type predominant, the opposite lower limb being affected for a few days, during which period it assumed the paraplegic type.

However this may be, the paraplegic form of local tetanus may assume two clinical aspects, accordingly as the localisation is in the upper or the lower limbs. These are: (1) the superior paraplegic type; (2) the inferior paraplegic type.

Symptomatology

The signs of the onset, whichever form of the malady is in question, are identical with those observed in

monoplegic tetanus. In this connection we refer the reader to the local and general modifications mentioned in the preceding chapter.

It must be remembered that in this variety it is principally the late-appearing form which is encountered; the period of incubation is almost invariably long: a fortnight, three weeks, or more.

(*a*) *Inferior Paraplegic Type.*—The inferior paraplegic type is by far the most frequent. The lower limbs are the seat of convulsive jerks of incredible frequency, still further exaggerated by the slightest emotion, the slightest agitation, the least shock or vibration.

In the period of acme paroxysms with remissions are observed. The attitude of the members has been well described by Demontmerot. The limbs, he states, are in forced extension, the foot strongly depressed, the instep salient, the toes usually turned under. Altogether, the foot reproduces with a fair degree of exactness the attitude of talipes equinus.

The muscles of the calf are stretched to the maximum, giving on palpation the sensation of an extremely hard, solid cord. The lower leg itself is extended to the maximum, the patella firmly immobilised, while the thigh is in extension upon the pelvis.

In most cases the contracture invades, at least, the lower abdominal muscles, so that the belly is enclosed by a hard, unyielding wall. Despite the importance which Bérard and Lumière are inclined to attribute to it, we have seen what prognostic value should be attached to this sign in connection with the monoplegic form. No amount of effort will restore the movements of flexion to the various segments of the limb, but the entire lower limb, fixed in extension,

may readily be lifted in one piece, as it were, by the toes.

This muscular rigidity becomes accentuated very rapidly, so that, apart from any convulsive paroxysm, and after the paroxysms themselves have disappeared, the lower limbs are absolutely immobile.

When this form is unmixed, leaving the patient the free use of the upper limbs, the superior vertebral articulations, and the muscles of the face, it gives the patient an appearance which is completely characteristic.

It seems as though the lower half of the body has suddenly been transformed into a lifeless mass, so that one has before one's eyes one of those fantastic mythological beings created by the Oriental imagination, the upper half of whom, being mobile and alive, offers a striking contrast to the lower half, which is immobile, and, as it were, petrified.

(*b*) *Superior Paraplegic Form.*—In the superior paraplegic form, of which only one case is known (Demontmerot), the upper arms, forearms, wrists, and hands were in forced flexion. The phalanges were folded down upon the palm of the hand, the thumb inserted inside the phalange of the forefinger, and strongly compressed by it ; the distorted hand was drawn violently down toward the forearm by the flexion of the wrist ; the forearm, which was stiff, with the integuments raised by the tendinous cord of the flexor muscles, made a very acute angle with the upper arm ; lastly, the upper arm was closely pressed against the thorax.

This position, carried to its extreme during paroxysms, presently persisted apart from these and, as in the inferior form, prohibited any use of the limbs.

In both types the development of paroxysms causes violent pain in the members affected.

The reflexes remain normal; Demontmerot observed neither clonus nor exaggeration of the reflexes. The sensibility is normal.

Lastly, the general signs are not marked; there is only a slight elevation of temperature, the thermometer varying between 98·6° and 100·4° F.; but this slight temperature quickly disappears once the paroxysm is terminated. This comparative athermia constitutes, as we shall see, another sign of a benign development.

The general condition remains good; we need only mention the abundant sweats, and the absence, upon examination, of any special organic disorders.

Such—expressed in outline—is the usual condition of the patient in the paraplegic form of localised tetanus. Very rarely, however, is the clinical picture unmixed. We have already mentioned the unexpected appearance of generalised contractures, and in this connection we shall ask the reader to remember that there are, in addition to the true localised form of tetanus, two forms of generalised tetanus which writers on the subject have confused with the partial forms.

Sometimes the generalised contractures happen to mask, for a time, the initial paraplegic localisation; this is what we have described as "the classic form of tetanus with paraplegic onset."

Sometimes, on the contrary, tetanus exhibits an absolutely normal onset, with trismus, opisthotonos, and fever, and only subsequently does the affection more especially assume an increasingly definite paraplegic form. In addition to the classic tetanus paraplegic at the first onset, we must, therefore, recognise a generalised tetanus with *paraplegic development*, or a *secondary paraplegic form.*

Considering the evolution of these paraplegic partial forms, we shall at once perceive that it resembles that of the monoplegic form—that is, it is very slow—and we may distinguish four periods of development. Lastly, we may remark that the prognosis is favourable.

Diagnosis

In a late-appearing form of tetanus particularly—which means in the majority of cases—the total absence of a clinical history may for some days hold the diagnosis in abeyance.

It should always be an easy matter, after an attentive and thorough examination of the nervous system, to eliminate the paraplegias resulting from peripheral and radicular, or medullary, or cerebral lesions.

Three affections in particular, by their very similar initial symptomatology, simulate localised paraplegic tetanus with some exactness. These are, on the one hand, tetany and hysterical paraplegia ; on the other hand, cerebro-spinal meningitis.

We shall not insist upon the differential diagnosis of tetany and hysteria, which we mentioned when speaking of the monoplegic form.

This leaves us to consider cerebro-spinal meningitis, whose diagnosis is comparatively easy. It suffices to remember that the spasms are quickly replaced by paralysis, that there is intense headache, with photophobia, vomiting, and spinal pains upon pressure. The laboratory, moreover, provides us with exact information by the chemical and cytological examination of the cerebro-spinal fluid.

In cerebro-spinal meningitis lumbar puncture, which

should always be practised directly there is the slightest suspicion of the possibility of a meningeal reaction, yields a turbid fluid, sometimes obviously purulent, with an increase of albumin, polynuclear reaction, and the presence of meningiococci.

CHAPTER V

LOCALISED TETANUS OF THE ABDOMINO-THORACIC TYPE

This variety of partial tetanic infection is quite exceptional. In the whole literature of medicine there is only one record of such a case of late and local tetanus. It developed one hundred and thirty days after the wound, and after the preventive injection of 10 c.c. of antitetanic serum.

The rarity of an exclusive and late-appearing tetanic localisation in the abdomino-thoracic muscles is such that we have decided to reproduce the unique and highly interesting observation published by P. L. Marie.

Observation (P. L. Marie)

C——, aged thirty-one years, who had already, in January, 1915, received a traversing wound in the left arm, after which he was given 10 c.c. of antitetanic serum, was again wounded, on the 10th July following, by shell-splinters, which caused numerous wounds of the face, the scalp, the upper part of the thorax, the left arm, and the left lower leg. Nearly all were superficial and of very small dimensions. Three deserve special mention: the first involved the left eye, of which the cornea was perforated and the lower lid lacerated; of the other two, which were fairly extensive and penetrating, one was situated in the left forearm and one on the inner face of the left thigh. Two days after the wound 10 c.c. of antitetanic serum were injected, without anaphylactic symptoms. On the 13th July, at the *Centre ophtalmologique* in Rouen, enucleation of the eye was performed, followed, four days later,

by the incision of a phlegmon in the forearm, with extraction of a splinter. Finally several operations were performed with a view to blepharoplasty. During this time all the wounds had healed quickly, excepting that on the thigh, which left a small fistula which discharged very slightly.

About the 10th November the patient, until then in perfect health, began to complain of intermittent shooting pains in the abdomen, thorax, and loins, these pains being presently accompanied by persistent muscular contracture in the abdomino-lumbar region.

Suspecting an attenuated form of tetanus, chloral was prescribed (3 grammes per diem). However, far from improving, the condition became aggravated. From the 20th November sudden jerks occurred, spreading from the waist down to the feet, compared by the patient to electric shocks, occurring in paroxysms, which left the upper limbs unaffected. Finally, during the night of the 3rd December, disquieting respiratory disorders appeared : frequent respiratory pauses occurred, sometimes attaining a duration of fifteen seconds, followed by slight polypnœas. On the 6th December the patient exhibited an intense contracture of the lower portion of the trunk ; the abdominal wall, slightly retracted, was incompressible, and presented the stony hardness so characteristic of tetanus. This contracture was permanent ; it was no longer accompanied by pain, and was of constant intensity.

The period of paroxysms of painful contracture was replaced by analgesic muscular rigidity. The dorso-lumbar muscles were also contractured, causing a marked exaggeration of the lumbar curve. The patient was able to sit down only with difficulty, by gripping the edge of the bed with his hands ; and the pain quickly forced him to lie down again. When told to pick an object from the floor, he was able to do so only with great difficulty, by flexing the knees to the maximum, the trunk retaining its stiffness. There was no other contracture, excepting a bare trace of trismus, the incisors being still capable of a division of 1·2 inches. The patient complained of a slight stiffness when he tried to open his mouth widely, but he was able to eat, drink, and speak without difficulty. The back of the neck and the upper and lower limbs were perfectly supple ; there was no Kernig's sign, but the walk was embarrassed, the patient complaining that he could not throw his legs forward.

The tendinous reflexes, normal in the upper limbs, were strong in the lower limbs, but notably more exaggerated on the left; there was no ankle or patellar clonus. The cutaneous reflexes were also stronger on the left, particularly that of the tensor fasciæ lata. On the inner face of the left thigh, by the upper edge of the femoral condyle, was the orifice of the little fistula already mentioned, which had dried up about a fortnight previously, and was covered with crusts. There were no disorders of the sphincters; and the respiratory symptoms had not recurred. The general condition was unaffected; there was neither fever nor emaciation. It should be noted, however, that there was a slight acceleration of the pulse (92), and an obvious exaggeration of the secretion of sweat; the whole body was moist, and the face was covered with a veritable dew.

The patient was given 40 c.c. of antitetanic serum by subcutaneous injection, without any subsequent reaction, and 4 grammes of chloral, and, five days later, a further 30 c.c. of serum.

For ten days the condition of the patient remained stationary. The exaggeration of the lumbar curve diminished slightly, but the abdomen was still as hard as before. There were no spasmodic paroxysms, no respiratory troubles. The reflexes were still greatly exaggerated in the left leg. The temperature remained normal, the pulse was about 80, and there was no constipation.

The fistula intermittently discharged a few drops of serous fluid.

Thinking that a foreign body was helping to maintain the suppuration, and that it had perhaps played some part in the development of the tetanus, and was an obstacle to its cure, M. Marie had the region of the knee radiographed. In this way a small shell-splinter was discovered on the inner face of the articulation, $2\frac{1}{2}$ inches below the orifice of the fistula.

On the 27th December a third injection of serum was given (40 c.c.) in order to guard against the eventual danger of a mobilisation of germs when the operation was performed, and on the following day the projectile was removed under a local anæsthetic. It was enclosed in a small cavity with thick fibrous walls, covered with a small quantity of pus which contained, in the midst of numerous polynuclear

leucocytes which were more or less cytolised, bacillary elements of various dimensions. The immediate culture of the germs covering the splinter in glucose agar (stab cultures) resulted in the development of a multitude of microbic colonies. In twenty-two hours the medium broke up, without giving off any odour. An examination conducted by Dr Ch. Aubertin revealed large bacilli with square ends, Gram-positive, having all the characteristics of *B. perfringens*; long slender bacilli, Gram-negative; a few curved bacilli, like the septic vibrio; and lastly, some diplococci, Gram-positive, which were rarer.

From the 31st December began a definite improvement. The abdomen became slightly depressible, the lumbar curve diminished, and the separation of the incisors now amounted to nearly two inches. On the following days the improvement was very marked, the abdomen becoming more supple; and about the 7th January the abdominal wall had become completely relaxed, even when the patient lay completely extended; the exaggeration of the lumbar curve had completely disappeared, and flexor movements of the trunk were performed with ease. On the 15th January there was no longer any trace of the abdominal contracture, and the maxillary separation was two inches. The tendinous reflexes of the left leg were once more normal, but the test of the left plantar cutaneous reflex still determined an exaggerated contraction of the tensor fasciæ lata.

The patient left the hospital, cured, on the 15th January. Seen a month later, he was in perfect health.

In this observation the tetanus was therefore confined to the abdomino-thoracic muscles, sparing all the remaining groups of muscles, excepting the masticatory muscles, which, however, were only very slightly affected.

The tetanic infection entered the system, as M. Marie justly remarked, by the wound on the anterior and internal face of the thigh. The toxin here secreted ascended along the branches of the lumbar plexus, the femoro-cutaneous nerve, and the internal cutaneous

nerve, finally reaching the corresponding spinal segment. Although the lower limb on the wounded side did not exhibit any stiffness, it would none the less appear to have been slightly affected, since an exaggeration of the tendinous reflexes was noted.

The development of this particular form recalls, as we shall see, that of the early or late-appearing localised forms already discussed.

During a first period, in short, there were paroxysms of painful contractures and intermittent jerks, which in this case were localised in the abdomen, and which spread to the lower limbs. These contractures were accompanied by disquieting respiratory disorders, which were, however, transitory, and might very likely be attributed to the extension of the contracture to the muscles innervated by the intercostal nerves.

This first period was followed by a phase of analgesic muscular rigidity, characterised by the hardness so peculiar to tetanus ; the lower half of the trunk of the patient observed by P. L. Marie seemed transformed into marble.

Lastly, the phase of progressive and lingering resolution appeared.

While the disease was passing through these different periods of development the patient's general condition was good ; there was no fever and no marked acceleration of the pulse. There was nothing to remark but the hypersecretion of the sweat-glands : a sign of known significance in tetanus.

The pathogenesis of this variety is like that of the other forms of localised tetanus, whether early or late-appearing ; and we shall presently see that in these cases an important rôle must be attributed to previous immunisation. As the result of an insufficient initial

preventive injection, or rather the insufficiency of a single preventive injection in respect of a prolonged incubation or a secondary reinfection, the tetanus assumes a clinical aspect which is local, attenuated, and benign. The incomplete or partial immunity conferred limits the development of the tetanic symptoms, without, however, preventing the fixation of the toxin in certain medullary territories.

Finally, the prognosis of this variety, like that of all the partial forms of tetanus, is benign.

CHAPTER VI

ATTENUATED FORMS OF TETANUS, WITH SLOW DEVELOPMENT AND PROLONGED INCUBATION

In addition to the monoplegic, paraplegic, and abdomino-thoracic forms which we have already described, we think it proper to mention the attenuated forms, with slow development and prolonged incubation, to which MM. Claude and Lhermitte have called attention, although these are not always partial varieties of tetanus. Our principal reason for mentioning these forms is that the disease presents such peculiar features that these may well deceive an observer who is not sufficiently forewarned.

In three of the cases reported by Claude and Lhermitte, in which the subjects were young, hardy soldiers, whose usual health was good, tetanus followed upon extremely superficial wounds of the limbs, inflicted by shell-splinters, making its appearance more than two months later than the date of the wound. There was nothing to lead one to expect the imminence of so serious a complication. The wounds, indeed, were by no means important, having suppurated only slightly, and being completely cicatrised, in two of these cases, a long time before the development of the first symptoms.

These latter consist of a slight stiffness, either of the muscles of the wounded limb, or, to begin with, of the masseters. These slight contractures permit the convalescent to perform the occupations of everyday life

without any particular difficulty; then they become more clearly defined, increasing in severity, and extending to other areas. At this stage the muscles involved are no longer those of the wounded limb, and the masseters, but the musculature of the neck, and sometimes even that of the trunk. Nevertheless, the patients are still able to walk with ease, and their general condition is excellent; they are, as a rule, regarded as suffering from neuropathic contractures.

When we examine such patients we are at once impressed by their peculiar and rather abnormal facial expression. The features appear as though congealed, and are unusually prominent; the eyes are half closed by motionless, narrowed eyelids; the mouth is pinched, and the neck is rigid; when the patient is stripped one is struck by the prominence of the sterno-mastoid and cutaneous muscles. The latter are rendered even more obvious if the patient be told to open his mouth; all the muscles of the face and neck contract, and the slender bundles of the cutaneous muscles are plainly outlined under the skin. The patient finds it difficult to open the mouth or protrude the tongue. The latter is thickly coated, and is marked with the imprints of the teeth; the breath is fetid.

The same hypertonia may be observed in the muscles of the lower limbs, whose movements are slow and painful; the upper limbs are free from this contracture, unless the initial wound is situated in one of them.

As a general thing this condition of muscular hypertonia is not interrupted by paroxysms of contracture, as in the classic form of tetanus, or else these paroxysms are extremely transient and difficult to detect. However, in two cases Claude and Lhermitte observed

paroxysmal crises, which spread to a large number of muscles, and which were extremely painful.

The general condition remains excellent, and the temperature shows no departure from the normal, or exceeds it but slightly.

This attenuated form of tetanus is accompanied by excessive hyper-excitability of the muscles and nerves to electrical stimulation, and an exaggeration of the osseous and tendinous reflexes, with clonus of the foot and saltation of the patella. In the neck, percussion of the insertions of the sterno-mastoids or the cervical trapezius causes a sharp and sudden contraction of these muscles ; in two cases percussion of the zygoma caused a sudden extensor movement of the head. These modifications of the reflexes are to be observed in the monoplegic form also, and in speaking of the latter we laid stress upon them as a differential sign distinguishing tetanic from hysterical contractures. In this connection also the hyper-excitability of the muscles and nerves under electrical stimulation, and the exaggeration of the osseous and tendinous reflexes, which is observed several weeks after recovery, constitute indications of the greatest importance in the difficult differential diagnosis of these attenuated and late-appearing forms and of hysterical contractures. The attenuated variety of tetanus, whose essential features we have just outlined, constitutes a highly individual form of the disease, by reason of its clinical phenomena no less than its slow development, its prolonged incubation, and the benign character of its prognosis.

CHAPTER VII

ETIOLOGY AND PATHOGENESIS

I. Etiology

Frequency.—The generalised form of tetanus, whether early or late, has long been known ; it is, comparatively speaking, a frequent affection. Localised tetanus, on the other hand, is excessively rare, and the number of definite observations is very limited. It is enough to refer to the chief observations reproduced in this volume to realise that records of the partial forms, early or late-appearing, are infrequent and of recent date. This, as we have already explained, may be largely due to the fact that the partial forms of tetanus were for a long time misunderstood, so that clinicians who were not familiar with them referred the localised contractures which they observed as following traumatisms to another cause. There is no need to read the old writers to realise the truth of this assertion. In Follin's *Traité de Pathologie externe*, published in 1867, that writer described, under the name of secondary traumatic spasms, an affection very similar to that which we have described : traumatisms were followed by convulsions confined to one member, with absence of trismus, and a fatal termination. Probably Follin had in his possession documents which enabled him to sketch the history of these traumatic spasms, and these latter, which by us are regarded as partial forms of

tetanus, are doubtless less rare than might be supposed. Their rarity, however, is explained by the undoubted fact that certain peculiar conditions are required for their development, and also by the fact that under certain conditions attenuated toxins may be developed, as we shall see when discussing the question from the pathogenic standpoint.

Cause.—The cause of localised tetanus of the members consists, as in all the other varieties of the disease, in the introduction into the system of the toxins secreted by Nicolaïer's bacillus, with which a wound has been infected.

Causal Agent.—The bacillus of tetanus was discovered in 1883 by Nicolaïer, in the pus of animals which he had rendered tetanic by inoculation with small quantities of earth.

Kitasato first isolated and cultivated it, and by demonstrating that inoculation with cultures of the germ gave rise to tetanus he proved its specific character. The important labours of Vaillard, Vincent, and Rouget determined the conditions under which tetanus is able to develop. Finally, the study of the toxin secreted by the tetanic bacillus enabled Roux and Vaillard to obtain a serum whose preventive action no longer calls for proof.

Morphology.—In the pus of the tetanic wound the bacillus occurs in the form of a rather slender, elongated rod, the ends of which are not rounded. It measures, on an average, 4 μ in length and 0·3 μ to 0·4 μ in thickness. It is usually devoid of spores.

In cultures its aspect differs according to the age of the latter.

During the first few hours of its development in bouillon it presents the same form as in pus ; but at the

end of eight hours it begins to sporulate. The tetanic bacillus then appears as a slender rod bearing upon one of its extremities a spherical, refracting spore, which gives the germ the form of a pin. At the end of a few days all the bacilli have sporulated. About the tenth day the bacillus proper atrophies, and later still it disappears from the culture, leaving only the spores.

Mobility.—Examined in the fresh state, in the absence of oxygen, the bacillus which has not yet sporulated is slightly mobile. Its movements are slow and sinuous. As soon as the spore has formed this mobility disappears.

Staining.—The basic aniline dyes will stain the tetanus bacillus satisfactorily. The sporulated bacilli take the stain only in their bacillary portion ; as for the spore, only the outline is stained, the centre remaining colourless. To stain the central portion of the spore one must employ the special methods for the staining of spores (Moeller's process, for example). The tetanus bacillus is Gram-positive.

Lastly, before the spore has formed the bacillus is provided with numerous vibratory cilia, which are attached laterally.

Cultures.—The tetanic bacillus is readily cultivated in anærobic media, but cannot support the presence of any very appreciable quantity of oxygen. The usual media may be employed, provided they are prepared with fresh bouillon (Kitasato). It does not readily multiply in media with albuminous bases, but cultures made in rabbit serum are extremely virulent.

In bouillon, after twenty-four hours, a homogeneous turbidity is observed, which continues for some days ; about the fourteenth or fifteenth day the culture sinks to the bottom of the tube and the liquid becomes clear. From the first day bubbles of gas are seen on the surface.

These cultures give off a disagreeable odour, recalling that of burnt horn.

On gelatine cultures obtained by deep punctures (to avoid the deterrent effect of oxygen) and maintained at a temperature of 20° C. the cultures make their appearance about the fifth day. In the region of the puncture cloudy spots are formed, from which fine needle-like formations extend in a perpendicular direction. These cultures spread more and more, until about the tenth day the gelatine liquefies in the lower portion of the tube, remaining intact in the upper portion.

The isolated colonies occur in the form of tiny spheres, of a cloudy appearance, from which grow tufts of fine needle-like filaments; these colonies are surrounded by tiny bubbles of gas. When, on the tenth day, the gelatine liquefies, the colonies appear as tuft-like formations swimming in a round cupule of liquefied gelatine.

On agar the culture is cloudy, without any very distinctive characteristics. The medium is broken up by numerous bubbles of gas.

On potato the development is poor.

In milk the cultures develop readily, and the medium is not coagulated.

Biological Properties.—Vitality.—The spores of the tetanus bacillus are highly resistant. Heated in a closed flask in a moist medium, they will support boiling for four or five minutes without perishing; while they resist a temperature of 80° C. for as long as six hours.

Dried in an albuminous medium (serum, blood, etc.), Maljean found that they frequently survived heating to 40° C. in steam, under pressure, for fifteen minutes.

If protected from the air and light, their vitality persists for several years. Mingled with blood or pus,

and sheltered from the light, they retain their virulence for a long time.

Mocard has found them living after a lapse of eighteen months upon articles which had been employed in connection with colts which had died of tetanus.

Eiselberg succeeded in giving tetanus to an animal by inoculating it with a splinter which had been extracted from the hand of a tetanus patient, and had been kept for two and a half years in a cupboard.

Formation of Indol.—Cultures in bouillon are rich in indol.

Formation of Gas.—The gases which are given off by the cultures are nitrogen, hydrogen, and hydrocarbons.

Hæmolysin.—According to Ehrlich and Madsen, filtered cultures of tetanic bacilli contain a substance differing from the toxin, which dissolves the red blood corpuscles of the majority of the domestic animals. This tetanolysin is very unstable ; it is rapidly destroyed if heated to 50° C. (in twenty minutes) ; exposed for five hours to a temperature of 20° C. it loses half its power, only a temperature of 0·0° C. enabling it to retain its activity for twenty-four hours. Tetanolysin is precipitated by sulphate of ammonia. The resulting powder, if desiccated, keeps for a long time.

Agglutinability.—The bacillus, as we saw when considering the diagnosis of tetanus, is not agglutinated by the serum of a human being or an animal suffering from tetanus. With the serum of a horse vaccinated against the tetanic toxin agglutination may be effected by very minute proportions : 1 in 2000 and even 1 in 5000 (Courmont).

Experimental Pathogenic Action. — Animals, in general, are susceptible to the tetanic infection. In the

laboratories the mouse, rat, and guinea-pig are employed by preference; the dog is highly refractory, while the domestic fowl and the pigeon are completely so.

To obtain experimental tetanus it suffices to inject under the skin or into the muscles of the thigh of a susceptible animal a small quantity of some medium containing tetanic bacilli or spores.

Inoculation with Tetaniferous Pus or Soil.—Pus collected from a tetanic wound is inoculated under the skin of an animal. At the point of inoculation a more or less extensive tumefaction is produced. Three or four days later contractures appear, first in the neighbourhood of the region inoculated, but later they become generalised; convulsive attacks occur as a result of the slightest excitation. The animal succumbs thirty-six to forty-eight hours after the onset of tetanus.

At the autopsy a purulent centre is discovered at the point of inoculation; this contains, in addition to the germs of suppuration, a few specimens of tetanus bacilli. This pus may, with success, be employed to inoculate other animals, but after three such passages the results are negative (Vaillard).

The viscera appear normal, except for a passive pulmonary congestion due to pre-mortal dyspnœa. By injecting tetaniferous soil under the same conditions, the same results are obtained; but at the point of inoculation a dry eschar is often produced, or a pseudo-membranous exudate due to the existence of associated germs.

Inoculation with Pure Cultures.—Subcutaneous, intramuscular, intravenous, intraperitoneal, or subdural inoculation gives rise to a typical tetanus. The

introduction of the germ by the digestive tract produces no result.

Young cultures, as a rule, are not very tetanigenous, as they contain but little toxin.

It is interesting to note that in all cases, no matter what the mode of inoculation, the blood remains sterile.

Tetanus Toxin.—The bacillus does not become generalised. The general signs are due to the action of a poison elaborated by the germ and diffused throughout the organism. The existence of this toxin was demonstrated for the first time in 1890, by Kund Faber ; it has been very fully investigated by Vaillard and Vincent.

Method of Preparation.—The tetanus bacillus is inoculated into a spherical flask containing fresh peptonised bouillon. This is placed in an incubator, which is kept at a temperature of 37° C. for eighteen to twenty days. It is then filtered through a Chamberland filter ; the filtrate obtained exhibits an alkaline reaction, and gives off the characteristic odour ; it is highly toxic, for a dose of ·001 c.c. kills a mouse.

Nature and Properties of the Toxin.—The earliest investigations gave rise to the hypothesis that the tetanic toxin was a ptomaine (Brieger). Others attributed to it the properties of the alkaloids. Ehrlich considered that it was composed of several substances : one being tetano-spasmin, an energetic convulsive agent, and another tetano-lysin, possessing no tetanising properties. In reality, the tetanic toxin may be likened to the diastases. Like them, it is greatly modified by exposure for half-an-hour to a temperature of 65° C., and exposure for three hours to a temperature of 80° C. kills it.

In a closed vessel, protected from light and air, it

may retain its toxic power for four months. Exposed to the air for one month, it loses a great part of its activity ; and the action of the air is greatly accelerated by the simultaneous action of sunlight.

Evaporated in a vacuum over sulphuric acid, at ordinary temperatures, the toxin is reduced to a brown residuum, amorphous and highly toxic. If absolute alcohol be added, the latter dissolves a portion of the residuum, which after evaporation is non-toxic. The portion insoluble in alcohol is freely soluble in water, and readily produces tetanus in animals. The dialysis of this tetanic substance is a rather slow process. Lastly, like the diastases, the tetanus toxin adheres to the precipitates of phosphate of calcium and aluminium which are thrown down from it upon the addition of chloride of calcium ; if these are carefully washed in sterile water and inoculated under the skin of the guinea-pig, the latter contracts tetanus.

According to Courmont and Doyon the tetanus toxin is merely a soluble ferment, devoid of toxicity in itself, but able to cause a fermentation of certain substances in the organism ; the true toxin results from this. This interpretation has not been accepted by other writers. Lastly, the toxin may sometimes be found in the blood of tetanic patients.

The Mode of Action of the Toxin.—The tetanic toxin is a poison of the nervous system, its special affinity for the latter having been demonstrated by the classical experiment of Wassermann and Takaki. The toxin was mixed with pulped cerebral matter, and subjected to centrifugalisation. The resulting liquid was devoid of toxicity, although the toxin was not destroyed. Roux and Borrel proved that it was fixed and immobilised by the nervous system, and then,

accordingto Metchnikov, absorbed and digested by the leucocytes.

The investigations of A. Marie show that the toxin attacks the nervous system in two ways. One portion of it passes into the circulation, where it is fixed by the nerve-cells; the other portion is absorbed by the peripheral nervous filaments, which gradually carry it, along the axis cylinders, to the nervous centres.

Habitat of the Tetanic Bacillus.—Now that we have considered the tetanic bacillus and its toxin, we have still to inquire into the habitat of the bacillus—a question of particular importance from the purely hygienic point of view.

Very often the occasional circumstances of the traumatism throw light upon the etiology of the disease. For the rest, the following remarks apply equally to all the clinical varieties of tetanus:

The Soil.—All authorities are at present in agreement as to the telluric origin of the tetanus bacillus. The spores of the tetanus bacillus are frequently found in the excrement of the horse. It is already some time since Sanchez-Toledo and Veillon proved that the tetanus bacillus is a frequent inmate of the intestine of the herbivora, and in particular of the horse. The bacillus, accordingly, occurs principally on the surface of the soil. At a depth of twelve inches it is rarer; on the other hand, it swarms in manure, or on dung-hills. In the present war the infection may be derived from the wound itself, which is contaminated by dust, or even by particles of earth (owing to the ricochet of bullets or shell-splinters). It may also occur directly, at the moment when the wounded man falls to the ground, or while he is lying on it. Infection may also be due to clothing covered with earth or mud which

contains tetanic germs. Or again, infection may be directly effected when the wounded man crawls over the ground in search of cover. It is probable that the great frequency of tetanus in the present war is due to the extensive earthworks necessitated by trench fighting.

It must be remembered that the soil contains more or fewer bacilli in different regions. There are tetanigenous centres—that is, centres where tetanus is more frequent than elsewhere. This fact has long been noted by veterinary surgeons, and is abundantly proved by a survey of the cases of tetanus which have occurred during the present war. Belgium and the regions at present invaded are said to be tetanus countries. Dr Paul Guillon states that the Marne contains tetanic belts—that is, districts where tetanus frequently occurs —while elsewhere it is of infrequent occurrence. It has been stated also that the soil of the Aisne valley contains far more tetanic germs than the soil of the surrounding districts. According to Bowby, tetanus was less frequent after the battles around Ypres than in the valley of the Aisne. Possibly the germs, like the flora, are affected by conditions arising from the mineral composition of the soil. The rich clay of Flanders is perhaps less propitious to the cultivation or dissemination of tetanic spores than the dusty, calcareous soil of Champagne. Let us note, lastly, that it is said that in England wounds are infected chiefly by staphylococci and streptococci, while in France one finds principally anærobic microbes, the tetanus bacillus, the bacillus of gas gangrene, and the bacillus of malignant œdema (Dutertre).

The existence of soils rich or poor in tetanic spores has been scientifically verified. There are no pure cultures of tetanic germs in the soil; perhaps it is to

the association of the germ with other microbes that the extraordinary virulence of the tetanus bacillus is due, when found in mixed infections. The importance of these microbic associations has long been known. Because of these associations, or the presence of foreign bodies, or again as a result of the attrition or destruction of tissues, the phagocytes, being otherwise employed, fail to prevent the microbic invasion. These associated microbes favour the tetanic infection.

Straw.—We must not fail to remark that while contact with the soil is dangerous, contact with straw which has been more or less contaminated by the ground upon which it has lain may also become a source of infection.

The manner in which the wound is inflicted.—The foregoing considerations explain the varying frequency of this complication according to the cause of the wound and the manner in which it is inflicted. It is obvious that there is every probability that the bullet which has not ricochetted carries no tetanic spores with it. This is not the case with splinters of percussion shells ; the shell having burst in the ground, its splinters almost invariably carry particles of earth with them, as does the ricochetting bullet. Doubtless in pursuance of this idea it has been said that tetanus almost always occurs as a result of wounds caused by artillery projectiles.

Any extensive wound of the soft tissue should be regarded as suspect.

Bullet wounds also yield a high percentage of tetanus (Dutertre).

Among 129 cases of tetanus Bazy cites, from the German periodicals, 9 cases due to rifle bullets.

Fragments having plane surfaces are more likely to

drag shreds of clothing into wounds than pointed bullets, which simply perforate the clothing when they strike point foremost; and we have seen that fragments of clothing contaminated by the soil may very well be the vehicles of tetanic spores. Although it is difficult to forecast tetanus, the manner in which the wound has been contaminated, and above all the carrying of shreds of clothing, with a mixture of grains of sand and little stones, into the wound, are valuable indications.

The situation of the wound is also an important factor, as will readily be understood. Wounds of the extremities are most liable to come into direct contact with the soil, and they are therefore most readily infected. The wounded man, in falling, throws his hands forward as far as possible; the man wounded in the leg or foot bears a wound peculiarly exposed to the dust rising from the soil.

Some statistics of Madelung's bearing upon the situation of the wound by which infection enters are significant in this connection. In 166 cases of tetanus the head was wounded five times; in 8 cases the trunk alone was wounded; in 50 cases the lower extremities only; while in 103 cases there were multiple wounds: wounds of the upper and lower extremities. In no case did tetanus result from a pulmonary wound: perhaps because of the richness in oxygen of the pulmonary tissues. The predominance of wounds of the lower extremities has long been known.

The Nature of the Wound.—This, perhaps, is not so important, in respect of the genesis of tetanus, as some would have it. Nevertheless, it is enough to examine the statistics, and we realise that tetanus is encountered more particularly in cases where there is great destruction of muscular tissue, and opening of articulations,

with abundant suppuration. In many of these wounds, moreover, at all events in this war, either shell-splinters are found, or fragments of straw contaminated by the soil, or shreds of uniform, with tetanic spores.

We have every justification for saying that while bullet wounds may give rise to tetanus, suppurating wounds of the lower extremities are predominantly those which are most frequently complicated by a generalised or localised tetanic infection.

Adjuvant Factors.—Atmospheric Conditions.—Heat is a factor which favours the tetanic infection. We know that when guinea-pigs inoculated with tetanic spores, without toxin, are placed in an incubator heated to 40° C. for two or three days, they contract a super-acute tetanus, developing as a sphlancnic tetanus, the bacillus being generalised through all the tissues. In the case of guinea-pigs infected thirty to sixty days previously, and then placed in the incubator under the same conditions, tetanus is still produced. These facts are explained by the destruction of the phagocytes under the influence of these high temperatures, this permitting the germination of the spores, which were immobilised in the leucocytes.

Cold.—Cold is also regarded as a factor favouring the appearance of tetanus, so care should be taken that a man seriously wounded does not become chilled.

Humidity is regarded by Schultze as a factor favouring the development of tetanus. We do not believe in the existence of this atmospheric influence, for the microbes occurring in dust are disseminated everywhere in dry weather, and find the conditions necessary to their development in the moisture of wounds.

Secondary Infection.—The part played by microbic associations in the production of tetanus is considerable.

This is proved by the experiment conducted by Vaillard and Vincent.

Under the skin of the guinea-pig were injected spores free from toxin, incapable of producing tetanus alone ; at the same time 0·5 c.c. of a culture of *microbacillus prodigiosus* was injected. Thirty-two hours later a mortal tetanus developed. It may be that the phagocytes seized upon the latter germ, ignoring the tetanic spores, which were able to germinate at leisure and secrete their toxin. This fact explains how soil which is extremely poor in tetanic spores may cause tetanus in man or beast, thanks to the common microbes which it contains, which play an important part in favouring the development of tetanus. This part, however, is not common to all germs. Vaillard and Vincent were unable to produce tetanus when the associated microbe was a staphylococcus, a streptococcus, *Bacillus subtilis*, or the pneumo bacillus. In order that a tetanic product may produce tetanus, the presence is necessary :

1. Of the tetanic bacillus, or tetanic spores.

2. Of a micro-organism capable of favouring its germination.

The Action of Chemical Substances.—According to Vincent, the salts of quinine act in the same manner as lactic acid, appearing to favour the tetanic infection when injected simultaneously with spores without toxin. Moreover, if in the case of guinea-pigs which have been inoculated with spores some days previously, and have remained healthy, a quinine salt be injected under the skin, tetanus breaks out, and the tetanic bacillus, which had remained in a latent condition, behaves as though attracted to the point where the quinine is injected, multiplies there profusely, and becomes generalised, even throughout the viscera. We

shall presently discuss the importance of this fact from the standpoint of prophylactic hygiene.

Direct Contact.—Lastly, there may be a danger of transmitting tetanus from one patient to another, hence the necessity of isolating tetanus patients and appointing special attendants. The present war has given us several confirmations of this etiological hypothesis. Dutertre records the history of three wounded men, who at Douai were placed in adjacent beds, and were attacked by tetanus. There is also the case of five wounded men who were put to bed in the same room, one beside another. Three of them had been infected in action ; forming part of the same regiment, and wounded at the same time, they had lain side by side on the battle-field. The three first gave tetanus to the two others, by touching their dressings with their hands.

We must add that the transmission of tetanus may also be effected by flies.

II. Pathogenesis

The history of the atypical forms of tetanus raises an interesting pathogenic question. It seems that in localised tetanus preventive serotherapy preserves the bulbar centres. The infection seems to be attenuated by incomplete serum immunisation. We know, experimentally, that an injection of toxin sufficient to provoke a generalised form of tetanus will give rise to an atypical form only if followed by an injection of serum within a period not exceeding two hours. In certain cases also there may be question of bacilli less virulent than normally ; the attenuated toxins would then act only upon the nerves of the injured member (monoplegic tetanus), or on one medullary segment

(paraplegic tetanus, tetanus of the abdomino-thoracic type).

This hypothesis is supported by the majority of those writers who have recorded cases of partial tetanus, and in particular by Pozzi, Carnot, and Laval : and it is all the more probable in that we are able, by injecting a weak dose of culture into an animal, to provoke contractures localised to the infected limb. In short, an atypical form of tetanus results. Thus if we inject, into the hind leg of a guinea-pig, an extremely weak dose of tetanic toxin, incapable of producing a fatal result, we obtain a typical local tetanus which is strictly confined to the inoculated limb. The contracture is rigid, and persists for some weeks. The action of the toxin does not proceed beyond the spinal cord segment innervating the inoculated limb, and exhausts itself there ; it does not attack other nervous centres. The comparison of such an experiment with actual clinical examples is always of the greatest interest. Klemm does not hesitate to assert that if we were carefully to observe wounded men who develop tetanus from the first, we should always find an initial local contracture in the region of the wound which admitted the tetanic infection.

As we have already remarked, in connection with our communication to the Academy of Medicine in January, 1916 (Obs. XVI.), there are two factors which enable us to explain localisation, early or late, in a wounded limb or a given anatomical region. These are, on the one hand, an incomplete preventive serotherapy ; on the other, the existence of bacilli of a low degree of virulence, few in numbers, and secreting attenuated toxins. These two factors may act in conjunction or singly.

Another question arises: What is the mechanism by which a preventive injection localises the tetanic infection? Is the virulence of the toxin secreted neutralised or attenuated, or does the preventive serum place the nervous system in a condition of defence, enabling it to check the ascendant progress of the toxin? This latter conception is plausible, and it seems highly probable, if we consider that the serum is preventive rather than curative, that the antitoxin, the moment it is injected, checks the further production of toxin, or, rather, destroys it as soon as produced in the region of the wound.

The secretion of the toxins being thus arrested, when the quantity acting upon the nervous system is the result only of a short lapse of time—the period dividing the moment of the wound from the moment of the injection—the dose in circulation is too small to become widely diffused, and to act directly upon the entire nervous system; it localises its action upon the nerves of the wounded limb and the corresponding spinal segments.

CHAPTER VIII

DEVELOPMENT AND PROGNOSIS

Development.—Generally speaking, the localised and atypical forms of tetanus and the partial forms of tetanus of the limbs are characterised by a slow development, with a tendency toward recovery. Owing to the long duration of the different periods of the infection, sequelæ may occur, veritable complications, which are usually of a transitory nature. Sometimes, however, these sequelæ are permanent, if the physician is not careful to guard against them or combat them directly they make their appearance.

The development of the localised forms of tetanus is sub-acute or chronic. It does not appear, to judge from the pathogenic conceptions expressed in the foregoing chapters, that an acute local tetanus can exist.

It is true that Vincent and Wilhem published, under the title of *Localised Tetanus*, details of a case of tetanus which was confined to the lower limbs, with contractures in hyper-extension, in which death occurred in twenty-four hours, as the result of grave pulmonary phenomena which were shown by an intense polypnœa. If this observation be analysed it plainly appears that the patient exhibited the signs of a tetanic infection which should rather have been classified as a super-acute generalised form of tetanus, in which the toxin was rapidly diffused throughout the system.

Owing to an extremely rapid development, the

clinical signs had no time to reveal themselves; the symptomatology therefore remained that of the more attenuated forms, giving the appearance of being localised.

As regards the monoplegic and paraplegic forms, whether early or late-appearing, we have seen that the period of incubation is fairly long: a fortnight or three weeks in general, and sometimes more. Once the first clinical signs make their appearance the disease develops through two or three well-defined periods. The first, which we have already described in detail, is characterised by a permanent contracture of one member, or of two symmetrical members, and by painful paroxysms affecting the same region. This first period lasts, on an average, ten to twenty days, sometimes more, as in our own observation.

A second period usually follows: a period of permanent, non-painful muscular rigidity. The contracture is no longer accompanied by painful paroxysms, and the permanent rigidity immobilises the patient as a complete monoplegia or paraplegia with extreme contracture would do. This is a period of long duration, and if we examine, for example, the observations published by Demontmerot, which deal with the paraplegic form, we find that in one case the rigidity persisted for twenty-one days; in another case for forty days; and in a third for forty-nine. Demontmerot regarded this second period, with its peculiar nature and long duration, as characteristic of the paraplegic form. However, it is nothing of the kind, for the same persistent stiffness of the limb attacked by the tetanic infection has been noted in the monoplegic forms. Courtellement, who was the first to publish an observation of tetanus localised in one limb, had already

insisted upon this point; and Pozzi's patient still exhibited this second period of non-painful contracture after the lapse of more than forty days. More than a month after the termination of the first period of development, Pozzi wrote that his patient's left lower leg was flexed at a right angle to the thigh by the powerful contracture of the flexor group of muscles, whose contracted tendons could be felt under the finger in the region of the popliteal space. There was also a slight contracture of the adductors. The extension of the leg was consequently absolutely impossible; moreover, the gastrocnemius was hard and rigid as a woody mass.

This period is often followed by a third and last period, during which the sequelæ of the preceding symptoms establish themselves, develop, or disappear. There may be a musculo-tendinous shortening; this is especially frequent in the gastrocnemius and the tendo Achillis, as in our own observation (XVI.). In the case described in this observation there was a very marked retraction of the tendo Achillis, which prevented the convalescent patient from placing his heel on the ground when walking. Trophic disorders, muscular or cutaneous, may be observed. Muscular atrophy in particular is frequent; it is sometimes slight and sometimes severe. Perforating ulcer of the sole has been observed.

Lastly, vaso-motor disorders may appear. These complications can, in some cases, be foreseen and obviated by early massage.

It will readily be understood that these complications involve a very long and troublesome convalescence, representing the fourth period of the disease.

It follows that the total duration of the malady in the monoplegic, paraplegic, and abdomino-thoracic

forms may amount to one, two, or three months, or even longer. In addition to these sub-acute forms, it will be remembered that there are forms even later-appearing, more attenuated, and longer in developing. Thus, in the attenuated forms, we have seen that the development is extremely slow, owing to the fact that the infection is attenuated by a previous preventive serotherapy.

Prognosis.—The localisation of the tetanic infection may be regarded as a sign of the benignity of the disease. It must not be supposed, however, that recovery is the rule. Partial tetanus is a serious malady, on account of the complications which may supervene, and the possible secondary generalisation of the infection.

The gravity of atypical tetanus is demonstrated by the observations of Routier. This author recorded three deaths among six patients. However, in the majority of cases, partial tetanus of the members develops in the direction of recovery, if we except the late-appearing post-operative forms, whose prognosis is not always so benign as that of the retarded forms which occur without operation. While in some cases the disease assumes an acute form, of the ordinary type, which is rapidly fatal, the usual progress of the disease is less rapid. The onset is commonly insidious, the contracture installing itself slowly and progressively, localising itself in the wounded limb, often accompanied by slight trismus and stiffness of the neck. No paroxysmal crises are observed, or only late-appearing paroxysms of little severity. Of the contractures, one of the most constant and persistent is that of the abdominal muscles.

The temperature is almost normal. Despite the

sub-acute form of the disease, and its insidious advance, the various signs which we have just recalled may finally become aggravated, terminating, after the lapse of several weeks, in contracture of the respiratory muscles and asphyxia.

According to Bazy, death occurs in one case out of two or three, according to the nature of the cases. But if we consider only the observations following upon operative intervention, the prognosis is even more gloomy; there were six deaths out of seven cases successively reported by Berard and Lumière, Querin, and Leriche and Desplas.

In atypical tetanus it seems as though we cannot seriously base our prognosis of the malady, or a forecast of its development, upon symptomatology. Although it is the rule, in the classical form of tetanus, to regard the prognosis as intimately connected with the length of the period of incubation and the temperature, this is no longer the case in the abnormal forms of tetanus.

The period of incubation, as we have many times repeated, is extremely variable. It may be long or short, but the prognosis does not appear to be affected thereby. We will merely remind the reader that the localised forms of tetanus, and their pathogenesis enables us readily to understand this, do not develop, as may happen with the ordinary forms, within a few hours of the wound; a fact which explains why the symptoms never appear in a tumultuous fashion, rapidly followed by death. But the indications furnished by the duration of the incubation period must not be regarded as absolute, even in the classical form. Thus Vautrin, addressing the Society of Medicine of Nancy, reported cases of acute tetanus whose onset was extremely tardy—the periods of incubation being

twenty-two and fifty-four days. Comparatively benign cases with a brief period of incubation are, however, very exceptional.

In the classical form of tetanus the temperature is, as a rule, a great help in establishing the prognosis. We know that pronounced hyperthermia and extreme frequency of the pulse are unfavourable signs. In the abnormal forms, and especially in partial tetanus, conclusions drawn from an examination of the temperature are, as we have already explained at some length, of little value. The two examples reported by Routier are a striking proof of this assertion ; in both cases the temperature never rose above 102·2° F., yet death supervened : in the one case fourteen days after the commencement of the tetanic symptoms, and in the second case two days after the appearance of a slight trismus, and painful contractions in the region of the elbow. However, it sometimes happens that the temperature furnishes no indications, even in the purely classic form of tetanus. A case has been recorded in which the temperature never exceeded 100·4°, and the pulse 90 to 96 per minute, but which terminated in death, despite the apparent benignity of the general symptoms. The acceleration of the pulse and respiratory disorders are elements of gravity even in the partial and atypical forms.

A pulse which is now almost normal, now very rapid, and a jerky respiration, are reasons for reserving the prognosis.

The permanent and progressive contracture of the abdominal muscles is, as we have stated, an almost constant symptom in the partial forms of tetanus; and according to Bérard and Lumière it should be regarded as of great importance from the prognostic point

of view. We know that these writers regarded this contracture as the prelude to contracture of the respiratory muscles and asphyxia.

With Routier, we do not believe that the prognostic importance which Bérard and Lumière attribute to it should be attached to this sign.

Still, one should always look out for this contracture, as when associated with modifications of the pulse and the temperature it may give us reason to forecast a fatal termination. We repeat once more that as this symptom is almost the rule in cases of partial tetanus, whose prognosis is, after all, comparatively benign as compared with that of the normal and usually observed form of the disease, its presence must not be regarded as a prime factor in the establishment of a positive prognosis.

To judge of the probable termination of a case of abnormal tetanus, we must also consider how far the deglutition and the functions of the larynx are affected. Again, the favourable action of narcotics upon the cramps should be regarded as a favourable sign.

Finally, if we are to believe Dr H. Gordon (*The Lancet*, 31st December 1914), the prognosis is peculiarly dependent upon the association of the tetanic bacillus with other virulent bacteria, and especially with the anærobic bacilli of Welsch. We know, too, that tetanus is frequently associated with gas gangrene, the bacilli of both diseases being anærobic.

To sum up: The abnormal forms of tetanus owe their benignity to their localisation, but they none the less constitute a serious malady, which necessitates prompt treatment; and this treatment, as Étienne observes, must combat the three phases of the disease: infection, intoxication, and cellular reaction. In spite

of everything, therapeutics, which calls for combined treatment, may prove inactive, when the disease terminates in death from asphyxia, due to the tetanus of the respiratory muscles, although the muscular contractures may not have become generalised. Death is not always the result of the contracture of the respiratory muscles, and Quincke even claims that in many sufferers from tetanus it results, on the contrary, from the complete relaxation of the respiratory muscles—that is, from their paralysis.

It is also certainly the case that death may be the consequence of a secondary generalisation of the tetanic infection: in other words, of a septicæmia, of a tetanic poisoning, or even of a pulmonary complication, such as the pneumonia of deglutition.

CHAPTER IX

TREATMENT

We propose to describe, in this chapter, the various treatments which have been successively recommended for the prevention of tetanus, and to cope with the disease when developed.

All that follows may be applied to the classic forms as well as to the atypical varieties of the tetanic infection. We shall give a brief final summary only of such matters as have especial reference to the abnormal forms, and shall indicate the treatment which appears to us most rational and efficacious.

We shall consider successively :

1. The prophylaxis of tetanus.
2. The treatment of tetanus properly so called.

First of all we shall emphasise the necessity of local treatment—that is, the treatment of the wound, by which the infection enters the system—and shall then proceed to deal with the general treatment, which should be specific and symptomatic.

Prophylaxis of Tetanus

We have seen that Nicolaïer's bacillus remains generally localised in the wound, and in the wound the toxin is manufactured. It follows from this that the prophylaxis of tetanus, which must be local and general, is based upon two fundamental principles :

(*a*) The complete cleansing of the wounds.

(*b*) Preventive antitetanic serotherapy.

Local Treatment of the Wounds

It is absolutely necessary to attend to every suspicious wound; to rid it of the tetanic bacilli which may have contaminated it, and to prevent the subsequent growth of the germs.

An extensive cleansing of wounds should always be effected, removing the particles of earth and the shreds of clothing carried into the wound by the projectile; lastly, a search must be made for any foreign bodies. In a word, the wound must be freed, as far as possible, from bacillary infection.

Amputations.—Obviously the means of cleansing a contaminated wound which at first sight appeared most effectual was to suppress it and replace it by a new, aseptic wound: hence the idea of amputating limbs with septic wounds. Thereby the introduction of fresh toxins into the circulation is prevented. Formerly, indeed, ablation and excision of the wound was recommended, and even the amputation of the extremities. It has fortunately been demonstrated that this procedure, which was indeed unduly radical, was ineffectual. Experience has shown that owing to the invasion of the nervous system by the toxin, mutilating operations can at most do no more than prevent the introduction of further toxins.

In our experience amputations do not prevent the outbreak of tetanus; even in cases of serious injury to the limbs this procedure, in our opinion, should be rejected.

The Search for Projectiles.—When these are not too deeply situated, they should be sought for as promptly as possible, with the aid of the X-rays or the various apparatus devised for the purpose of discovering foreign

bodies (Bergonié's or François' electro-vibrator, etc.). Foreign bodies may serve as the nidus for Nicolaïer's bacillus and the other anærobic germs which favour tetanic toxi-infection. By removing a shell-splinter, or a bullet, we diminish the probabilities of suppuration, and enable the cicatrisation of the wound to proceed more rapidly. Moreover, this procedure enables us to rid the wound of tetaniferous contaminations, and to avoid a secondary intervention, which may become, as Bérard and Lumière have shown, the occasion of renewed virulence on the part of the tetanic spores, and the origin of a late tetanus, localised or otherwise.

This search for foreign bodies offers, therefore, a two-fold advantage from the point of view of prophylaxis.

If we consider the cases of tetanus, atypical as well as classical, which have occurred during the present war, we find that asepsis and the mere cleansing of the wounds is not sufficient to prevent the development of tetanus.

Antisepsis.—In war surgery the antiseptic method must be employed. Although antisepsis is out of fashion nowadays, surgeons quickly realised the necessity of discovering antiseptics which would act upon the bacillus of tetanus.

Chemical Agents. — Tincture of Iodine. — In vitro tincture of iodine neutralises the tetanic toxin, but it must be remembered that in spite of the constant and systematic employment of iodine upon wounds received in battle, tetanus has appeared with comparative frequency.

Oxygen. Nicolaïer's bacillus being anærobic, the idea arose that it might be destroyed by bringing it into contact with oxygen. For this purpose oxygenated water was employed, and hyper-oxidised substances

which readily liberate oxygen. Oxygen, moreover, acts not only on the bacilli, but also on the toxins which they secrete.

This property of the tetanic germ, of developing in the absence of oxygen, known as anærobiosis, provides therapeutics with a valuable means of attacking the tetanus bacillus. Numerous preparations possess the property of liberating oxygen at the surface of a wound ; oxygenated water may be used in this way, or magnesium peroxide.

All wounds which have been contaminated by the soil, by shreds of dirty clothing, or by a foreign body, are suspect from the point of view of tetanus. Such wounds must therefore be cleansed with oxygenated water or powders which give off oxygen. The same with old wounds which have given rise to tetanic in fection : no good result can be obtained save by acting upon them with oxygen. The tetanic bacillus is killed by oxygen, and the gas, especially in the nascent state, slowly cleanses the wound, destroying toxins, detaching shreds of fat, clots of blood, and dead tissues, without ever exercising any harmful action (Dutertre).

Certain writers have, while experimenting, observed a fact of great interest and importance—namely. that the toxicity of various toxins is destroyed by the peroxides. They have succeeded, by means of oxygenated water and peroxide of calcium, in annulling the toxicity of a large number of toxins.

The same result may be obtained by means of ammonium persulphate. This is a powerful oxidising agent, which also possesses appreciable powers of disinfection. Unlike hydrogen peroxide and calcium peroxide, it may be employed in intravenous injections.

It has little toxicity ; a neutral salt, of a light base, it remains neutral while yielding its oxygen.

Oxygen acts not only upon the tetanus bacillus, but on its toxin ; hence its employment, not merely as a preventive, but also as a curative remedy. Wounds of a suspect nature, and wounds infected with the tetanic bacillus, should therefore be treated with oxygen.

Calcium Hypochloride.—According to certain writers, chlorine prevents the development of the tetanic bacilli and the production of toxins in the wound.

Despite these considerations, the various antiseptics have in reality hardly any effect upon the tetanic spores, whose powers of resistance, as we have seen, are considerable. On the other hand, they do act upon the ordinary microbes, the germs of suppuration, whose association with the tetanic bacillus is necessary to ensure its pathogenic action.

The employment of desiccated and powdered anti-tetanic serum has also been recommended in the case of extensive or lacerated wounds. But this procedure is far from sufficient alone as a protection against tetanus, unless it is seconded by the injection of the serum. In this connection Merieux found that a mixture of anti-tetanic serum and sub-gallate of bismuth, applied to a contaminated wound six hours after contamination, prevents the development of tetanus in the guinea-pig.

Physical Agents.—Hot or Cold Air.—Clinicians have conceived the idea of treating wounds suspected of tetanic infection by means of insufflations of air. The following treatment has been recommended : no sutures are made ; on the contrary, the wound is fully opened up ; lacerated, bruised, or mortified tissues are ablated as promptly as possible ; and the large wounds thus opened are treated by means of insufflations of hot air.

This procedure, which dries the wounds and stimulates the production of fleshy vegetation, has been employed with success by various surgeons.

Cold air gives the same result, but its employment is slightly painful.

We may also employ an intensive current of air in the prophylaxis of tetanus. It will be readily understood that the increased supply of oxygen carried by a powerful current of air into all the recesses of a wound prevents the development of the anærobic bacilli which cause tetanus.

These various procedures act principally upon the toxin, and it would be a matter of capital importance could we destroy this tetanic toxin by oxidation.

As a matter of fact, we already possess a means of destroying the tetanus bacillus itself, and thus of preventing the production of further toxin. The ultra-violet rays possess this bactericidal property.

Treatment by Light.—The action of the various rays of the solar spectrum, and of full sunlight, has long been utilised in the treatment of wounds in general. We know that under the influence of the ultra-violet rays wounds cleanse themselves and cover themselves with fleshy vegetation, while pain is alleviated.

The bactericidal action of light has therefore been employed in waging war upon the tetanus bacillus. Moreover, it has been proved experimentally that the toxin of tetanus is susceptible to the action of luminous rays, and that the spores are extraordinarily sensitive to the ultra-violet rays. Their employment should accordingly constitute one of the best methods of treatment.

In exposing a wound to light our principal motive is to excite an inflammation, an augmentation of the curative physiological processes.

This inflammation causes a hyperæmia and a serous exudation, of arterial origin, as well as an abundant proliferation of the tissues. The tetanus bacilli are therefore attacked in two ways: on the one hand, by a greater supply of oxygen in the tissues, caused by the inflammatory reaction provoked by the light; and on the other hand, by the bactericidal action of certain rays of the spectrum.

It is certain, in view of the bactericidal action of sunlight, as well as its curative action upon wounds, that our wounded patients, especially those suspected of tetanus, ought to receive as much sunlight as possible.

Contagion.—From the prophylactic point of view, it must be remembered that wounds which upon cultivation yield pure cultures of tetanic bacilli are not always complicated by tetanus. Analogous facts are well known to obtain in the case of other infections—in particular, of diphtheria and cerebro-spinal meningitis; and as in these infections, so in tetanus there are healthy carriers of the specific bacillus, who may become agents of contagion, if the surgeon neglects the strictest asepsis, and employs the same instruments in attending a number of patients.

There are no longer, in these days, "epidemics of tetanus," but their memory proves the necessity of subjecting all instruments to a prolonged sterilisation, preferably by means of the autoclave, in order that the tetanic spores may not be carried from one wound to another.

It must be remembered, also, that some years ago several cases of tetanus were reported after the use of gelatine injections, and the employment of catgut (cases reported in France and America), and of felt in plaster-of-Paris splints. Great care must therefore be

taken to sterilise gelatine and catgut, as these may contain tetanic spores.

The Action of Cold.—Lastly, cold being one of the factors which favours the appearance of tetanus, care should be taken that the wounded man is not chilled during transportation, and that he is warmed directly he enters the ambulance or hospital.

Preventive Serotherapy

Despite the various preventive treatments already discussed, despite the most rigorous precautions of asepsis and antisepsis, it must be admitted that it is almost impossible to eliminate from a wound the tetanic germs which may infect it.

To protect the wounded man against the toxins secreted, he must be given one or several preventive injections of antitetanic serum.

Antitetanic Serum.—History.—The serum of animals immunised by the injection of progressively increasing doses of tetanic toxin possesses properties which have been utilised in the prevention and the attempted cure of tetanus. Behring and Kitasato, in 1890, demonstrated the antitoxic powers possessed by such a serum.

In 1892 Vaillard investigated certain points relating to the serotherapy of tetanus. The blood of the fowl does not neutralise the toxin, but it becomes antitoxic about three weeks after an injection of filtered culture into the peritoneum. This property persists for eight months. Vaillard also demonstrated that Nicolaïer's bacillus vegetates and elaborates toxin in the serum of protected animals; that it multiplies in the living tissues of an immunised animal; and that it is not attenuated by the prolonged action of the lymph of a

protected animal. In short, the serum is only *antitoxic*; it is not bactericidal.

In 1893 Roux and Vaillard went into the whole question of antitetanic serum. They demonstrated, giving technical details, that the serum is more active *in vitro* than when injected preventively. The guinea-pig, which is given 15,000 lethal doses of toxin, mingled *in vitro* with an equivalent quantity of serum, is able to resist the toxin. But this quantity of serum would have been insufficient to protect the guinea-pig against 15,000 lethal doses of the toxin. The immunity due to the injection of serum is acquired immediately, but it lasts only for a few days. The conclusions of Roux and Vaillard as to the preventive and curative properties of the serum are explicit. Injected simultaneously with the toxin, or within a few hours, it transforms a generalised and mortal tetanus into a local and curable tetanus; injected at the end of the period of incubation, or after the contractions have commenced, it is absolutely ineffectual. Since then the antitetanic serum has been employed only as a preventive. Nocard ardently recommends its employment; meanwhile sufferers from established tetanus are still given the serum, and certain cases of recovery are published, which are, however, of a highly debatable nature.

In 1898 Roux and Borrel recommended the treatment of established tetanus by the intra-cerebral injection of the serum. We shall refer to this method again when discussing the specific curative treatment of tetanus.

Preparation of the Serum.—Horses are immunised against the tetanic toxin by injecting, in the first place, doses of the toxin attenuated by the admixture of a solution of iodo-iodide. These injections are repeated every three or four days. About the twenty-fifth day,

the serum already exhibits a certain antitoxic power, which is then greatly reinforced by subcutaneous injections of pure toxin (10, 15, 20 c.c., etc., every two or three days). At the end of six weeks about 50, 100, 150, or even 350 c.c. are injected into the veins.

The horse supports these enormous doses of toxin—two drops of which would suffice to kill a non-immunised horse—without injurious effects.

Ten days after the last injection the serum is collected by venesection. To maintain the immunisation, large doses of toxin are again injected at intervals of a few days.

The antitetanic power of the serum survives for a very long time—a year, and even more; it is, however, preferable to employ none but recent serum.

The serum may be preserved in the dry state. When required for use it suffices to dissolve the dry serum in six volumes of sterilised saline water, but it is better to use the natural antitetanic serum.

To avoid the slight toxic symptoms which may accompany the injection of any serum, the serum may be warmed for twenty to thirty minutes to a temperature of 138° F. It is then less irritant.

Properties of Antitetanic Serum.—Antitoxic Powers.—If an appropriate mixture *in vitro* of antitetanic serum and a mortal dose of toxin be injected into an animal, no tetanic symptoms develop, and the animal survives the experiment. Roux and Vaillard were able to obtain a serum which, as we have already remarked, neutralises 100 mortal doses of toxin for a guinea-pig in doses of 1 in 100,000 c.c.

This antitoxic power being proved, the above writers established under what conditions, and in what

quantities, it could be utilised to prevent and even to cure tetanus.

Preventive Power.—1. *Against the Tetanus Toxin.*—An animal is given a subcutaneous dose of antitetanic serum ; then, forty to sixty minutes later, a mortal dose of tetanus toxin. As we have seen, it exhibits no tetanic symptoms, and survives.

We know, moreover, having dwelt upon the fact when considering the pathogenesis of atypical tetanus, that if the serum and the toxin are injected simultaneously at different points, the two substances are diffused through the tissues with unequal rapidity ; the toxin outstrips the serum, and the small quantity which then escapes the action of the antitoxin suffices to provoke those slight, limited forms of tetanus, which are nearly always curable.

Finally, if the serum is injected after the toxin, but before the onset of tetanic symptoms, the tetanus is always local. The later the injection of the serum, the larger must the dose be, in order to prevent the generalisation of the infection, and to avert a fatal result.

2. *Against the Tetanic Infection.*—Against experimental tetanic infection the preventive power of the serum has greater scope for action, since there is always a certain interval between the moment of inoculation and the moment when the toxin enters the circulation. On the other hand, the poisoning is continuous, the bacillus continuing to secrete its toxin as long as it continues to live.

The injection of the serum before infection or at the moment of infection indubitably and completely confers protection upon animals.

If the serum is injected intravenously after infection, protection is assured on condition that the serum is

injected within forty-eight hours of the tetanigenous inoculation, and is employed in sufficient quantity. If the serum is given by intramuscular injection its preventive action is doubtful, by reason of the slower absorption.

The immunity conferred by the serum is only temporary. After its elimination from the system, about the twelfth or fifteenth day, the tetanic spores immobilised by the phagocytes, being no longer affected by the serum, are able to develop, and to pour the toxin into the circulation at a time when there is no longer any antitoxin to arrest or to hinder its action.

The proof of these experimental data was established by Nocard, who experimented upon the horse and the larger domestic animals. Certain accidents from which these animals frequently suffer (wounds from nails in the road, or wounds inflicted by the farrier, etc.), and operations, such as castration, the amputation of the tail, and the reduction of hernia, are often enough followed by tetanus. Out of more than 2500 animals given a preventive injection immediately after operation, not one contracted tetanus. Out of 6000 others, treated one to four days after the infliction of wounds contaminated by dung, soil, earth, nails lying in the road, etc., only one contracted tetanus. At the same time there were 315 cases of tetanus among animals which received no preventive injection.

Combining the statistics collected by Nocard, Labat, and Vallée, among 16,917 animals which were given preventive injections, Vaillard discovered only one case of tetanus. No more conclusive statistics could exist.

We shall presently see that the preventive power of the serum when administered to human patients is indisputable, and that the cases of tetanus in wounded

men who have been treated with serum have occurred in instances where the serum was injected too long after the infliction of the wound by which the infection entered, and in which the bacillus continued to grow and secrete its toxin, as the injections were not repeated after the elimination of the serum.

Now that we have learned the fundamental properties of the antitetanic serum, and before indicating the principles of preventive serotherapy, we will briefly insist upon the innocuousness of the treatment, and its efficacy.

It would seem needless, after the numerous examples provided by the present war, to devote any space to this subject. We have been induced to do so, however, by the comparatively recent discussion of serotherapy and its dangers, and in particular by the report read by M. Netter before the Academy of Medicine, during its session of the 2nd of May last. This writer, however, declared that serious symptoms resulting from a first injection (the serum sickness which we shall presently describe), or from reinjections (anaphylactic accidents) are very rare ; above all, if the injection is made in the subcutaneous cellular tissue. Moreover, it must be admitted that the fear of accidents ought never to deter us from having recourse to serotherapy.

Certain physicians and surgeons who have denied the prophylactic value of the serum, and who have further accused it of being the cause of distressing symptoms, have shaken the confidence of many practitioners, and it is in order to refute the arguments invoked against the use of antitetanic serum that we feel obliged to emphasise the innocuousness and the efficacy of preventive serotherapy. It must unhappily be admitted that many of the deaths from tetanus recorded at the

beginning of the war were due precisely to the erroneous ideas which had been expressed concerning the dangers of preventive serotherapy.

Innocuousness of the Antitetanic Serum.—Some have attributed to antitetanic serum a series of symptoms which are common to the various therapeutic serums. These are not due to any peculiar property of the antitetanic serum; and since the investigations of von Pirquet and Charles Richet these complications have been thoroughly understood. Discussing the accidents consequent upon serotherapy, we shall distinguish between those which follow a first injection and those which occur after reinjection. We shall describe, therefore, on the one hand, the serum sickness; and on the other hand, the anaphylactic accidents.

Accidents following a First Injection.—Between the eighth and the fifteenth day after a subcutaneous injection of antitetanic serum, and occasionally later, but seldom sooner, the patient may exhibit three symptoms, associated or singly: an eruption, pains, and a slight rise of temperature.

The eruption, localised in the region of the face, presently becomes generalised, and may assume one of several different aspects. The urticarial, pruriginous forms are most frequent; these consist of a diffused eruption of small or of moderate dimensions, or large red patches, which undergo progressive extension. Their aspect sometimes recalls the eruption of measles, or an erythema like that of scarlet fever. We have sometimes had patients sent to us as contagious cases, who were merely suffering from a serum eruption, as was demonstrated by the history and the development of the malady. In the course of the scarlatiniform serum erythema it should be remembered that desquamation

may occur in large patches, but in general it takes place earlier than in true scarlatina, and is not accompanied by angina.

Very frequently, too, the serum eruption is polymorphic; it then consists of a morbillo-scarlatiniform erythema with predominance of urticarial elements.

The pains are felt in the joints, but no local swelling is observed. Usually they recall simple arthralgia without tumefaction, and more rarely simple neuralgia, or myalgia.

The elevation of temperature is slight; the thermometer rarely rises above 100·5° F. Sometimes, however, as we shall see, it does exceed this figure.

This serum sickness, which is slight and without gravity, rarely continues for longer than four days. Its frequency varies greatly, according to the mode of preparing the serum; it is less common in France (where it occurs in 13 to 14 per cent. of cases) than in Germany, which is due to the fact that the French serum is heated to 56° C. Even when the mode of preparation is identical, the syndrome develops more readily when the serum of certain horses is employed. It is not possible to explain precisely why this should be so.

The serum reaction is occasionally more marked. The temperature rises to 104° F., which, in the presence of a morbilliform erythema, and, above all, of a scarlatiniform erythema, does not facilitate diagnosis.

In such cases delirium may be observed, and agitation, or even meningeal reactions, with headache, stiffness of the nape, and Kernig's sign. The kidneys may in turn be affected, a condition which will be revealed, upon testing the urine, by the presence of albumin, and clinically, sometimes, by œdema.

In a few cases the lymphatic glands are hypertrophied. This veritable serum sickness does not usually last more than a few days, but it leaves behind it a prolonged adynamia. Regnier has even published an observation of a case in which, a week after the injection of the antitetanic serum, pericarditis supervened, the sequelæ of which persisted for a year.

A few fatal cases have been reported. Thus, Riche reported the case of a child, observed by Rilhac, which was rapidly fatal, with hypothermia and Cheyne-Stokes breathing. The subject had received a preventive injection of 10 c.c. of antitetanic serum.

Other writers have been so far mistaken as to inquire whether the preventive injection might not in certain cases have determined the appearance of the clinical signs of tetanus. In the majority of such cases there were meningeal reactions, with pseudo-tetanic contractures: temporo-maxillary arthralgia producing trismus, or arthralgia of the vertebral column determining a stiffness of the trunk. Lastly, if we very carefully analyse the majority of the fatal cases observed subsequently to serum injections, we find that in certain instances death was attributable not to the serum, but to acute septicæmia due to a septic injection. In certain cases, moreover, an alteration or accidental contamination of the serum may be incriminated.

The symptoms which follow a first injection of antitetanic serum are explained by the well-known toxicity which any animal serum presents for an animal of another species when injected into the latter. We know that a heterogeneous non-antitoxic serum of any kind causes similar symptoms.

Marfan, however, would attribute a certain action to

the antitoxin. According to him phenomena of precipitation occur *in vivo* analogous to those which occur *in vitro* when a toxin is brought into contact with the corresponding antitoxin. The precipitants formed in the blood after the injection of antitetanic serum into a wounded man already intoxicated by the tetanic toxin give rise to capillary embolisms which might be the anatomical substratum of the symptoms.

This theory is not enough to explain the symptoms which occur in the case of numbers of wounded men who are not already infected by tetanus.

Symptoms due to the Reinjection of Serum.—These may be early or late-appearing.

Symptoms appearing some time after Reinjection.—These may be summarised as eruptions, pains and fever; they are of brief duration, and their prognosis is benign. They recall the symptoms which we have already mentioned as occurring after a first injection of serum, and differ from these only by a greater frequency and a shorter period of incubation. Thus in France they are observed in 50 per cent. of cases, instead of 13 or 14 per cent., and they appear two to five days after reinjection, instead of eight to fifteen days after the first injection, as we have already seen.

Their pathogenesis is probably the same.

Symptoms which appear soon after Reinjection.—The immediate symptoms, on the other hand, are peculiar to reinjection, and present special characteristics. They may be local or general.

The *local phenomena* often follow a benign development.

At the point of reinjection, and almost immediately after the serum is administered, a more or less marked

redness makes its appearance, or a painful œdema, or urticaria. These abnormal phenomena are usually of brief duration, disappearing in a few hours, or at all events in a day or two.

Nevertheless, a local gangrene may be observed at the point of reinjection, accompanied by serious general indications. Eight such cases, followed by death, have been reported in the course of an incalculable number of reinjections of serum. However, all these cases occurred in the course of anti-diphtheritic serotherapy, and death appears to have been due to the coexistence of a dangerous state of infection.

General Symptoms.—The general immediate symptoms consist of a rapid collapse with diminution of arterial pressure. This collapse varies in duration. But in infected and debilitated subjects these disorders, which are but slightly marked at the outset, become aggravated instead of attenuated. Two cases of sudden death have been reported, one after a reinjection of anti-plague serum, and one after the administration of anti-diphtheritic serum. The history of these very exceptional accidents is elucidated by that of experimental reinjection (Richet and Portier, 1902).

We must conclude, from the experimental data, that the subcutaneous reinjection of serum is less dangerous than intravenous or intracerebral reinjection, which may cause death within a few minutes.

It must also be remembered that the symptomatology of experimental anaphylaxis does not make its appearance unless injection and reinjection are separated by an interval of a fortnight. It varies, moreover, in different animal species.

In man the frequency of anaphylactic accidents has been greatly exaggerated. We shall refer to two

definite cases, when discussing the curative treatment of tetanus.

In a generalised and complicated infection it is difficult to distinguish the symptoms which are dependent on the causal malady from those due to the reaction of the system under the influence of serotherapy or the therapeutic agents employed. Only the immediate or late-appearing symptoms which we mentioned as occurring in man recall the anaphylactic accidents of animals ; the local gangrene which may be observed at the point of reinjection is analogous to the gangrenous phenomenon of Arthur, and the cardiac collapse to the anaphylactic shock. However, serious symptoms are exceptional, and some of them may be avoided by taking a few precautions.

In this connection Marfan has recently laid stress upon the abuse of injections of heterogeneous serums ; the abuse of serums whose efficacy is doubtful, such as the anti-streptococcic serum, which certain physicians recommend in erysipelas ; the abuse of specific serums injected for a non-specific object—for example, the injection of anti-diphtheritic serum, or ordinary horse serum, in severe hæmorrhage, diseases of the blood, ocular infections, etc. It must not be forgotten that the extension of serotherapy involves the risk, sometimes without the excuse of absolute necessity, of placing a large number of patients in a condition of hyper-sensibility in respect of serum reinjection which may be absolutely indispensable should they ever happen to be wounded, or to contract diphtheria, or cerebro-spinal meningitis, several months or years after the first injection of serum.

As it is the heterogeneous albumin which enters into action rather than the antitoxin, anaphylaxis occurs

indifferently when the injections, divided by a longer or shorter lapse of time, have been made with the same serums, or with serums differing in their antitoxins. Thus, a first injection of anti-diphtheritic serum or anti-meningococcic serum may become, on the occasion of an antitetanic reinjection, the origin of anaphylaxis.

Among the measures to be taken to avoid accidents, we must mention the preventive administration of chloride of calcium, in doses of 1 gramme per diem, and of adrenaline in doses of ten to fifteen drops of a 1 in 1000 solution. The adrenaline, whose hypertensive action is well known, will prevent or oppose the sudden fall of arterial pressure which is observed at the moment of the anaphylactic shock. These therapeutic agents, which are specially to be recommended on the occasion of reinjection in the curative serotherapy of tetanus, should be employed in preventive serotherapy when a few slight accidents have been observed at the time of the first injection, when the patient is infected and enfeebled, or when he exhibits a pathological taint. In a tuberculous patient, or one predisposed to urticaria, asthma, or hay fever, they should always be employed.

In all cases of wounded men who have previously, for any reason, received one or more injections of serum or serums, and in those cases especially in which anaphylactic accidents appear to be more readily produced, the anti-anaphylactic method of Besredka should be employed. This is based on the employment of small doses. If no marked anaphylactic symptoms are observed, it is possible, after a certain lapse of time, to inject large doses of serum without serious accidents. Thus, if in the first place we inject, subcutaneously, 0·5 c.c. to 1 c.c. of serum, we may, three or four hours later, inject the total necessary dose. This will be

given slowly, in order that the injection may be suspended upon the slightest threat of accidents.

Certain writers have recommended the addition to the serum of such substances as hydrochloric acid, iodine, sulphate of magnesium, formol, or chloroform, with the object of suppressing the effects of the anaphylotoxin. This method should be abandoned, for it has not given satisfactory results.

It follows, from these facts, that in practice these anti-anaphylactic precautions must be taken whenever it is possible to do so. It is obvious that in a dressing-station or field hospital, where there are great numbers of seriously wounded men, it is often impossible to discover whether the patient has previously received an injection of any kind of serum, or to wait three hours or longer between the injection of the small anti-anaphylactic dose and that of the massive dose which is required. In such cases there is no room for hesitation, it being a matter of urgency to inject all the wounded without distinction. Moreover, we are a hundred times more likely to expose the wounded man to the risk of tetanus by refraining from administering the preventive antitetanic injection than to produce serious anaphylactic symptoms by a serum reinjection which takes no account of his pathological past.

We have no hesitation in repeating that the fear of accidents following upon a seric reinjection, whether it has reference to tetanus, or cerebro-spinal meningitis, or diphtheria, has caused many more deaths than anaphylaxis itself.

The Efficacy of Preventive Serotherapy.—According to the opponents of the preventive serotherapeutic treatment, the serum is not only dangerous, but has no effect upon the final development of the disease. They base

their erroneous conceptions on the development of a few cases of tetanus, and their gravity, despite the employment of serotherapy.

Regnier, in this connection, reminds us that 41 cases of tetanus developed in spite of preventive injections, and that of 18 cases observed in France 13 were fatal. This figure, 41, taken from the statistics published by Vaillard in 1906, is by no means exaggerated, and Chattet, in 1909, increased it to 51. If we compare this figure with the numerous observations of cases which have developed in the absence of serotherapy, and if we subtract from it 19 cases which, according to a conscientious analysis undertaken by Chattet, should be regarded as doubtful or wrongly diagnosed, we see that such statistics are of little value as an argument against the genuinely efficacious character of preventive serotherapy, especially as we know that in some of the 32 cases on which we may rely the physician contented himself with powdering the wound with dried serum, a method which is recognised by all as blind and insufficient.

We have already referred to the eloquent statistics of the veterinary practitioners, and of Nocard in particular, concerning the importance of preventive serotherapy, and the results obtained by its employment. In human medicine also the majority of surgeons and physicians recognise that tetanus declares itself only when the preventive injection has been omitted. Moreover, the colonial wars have proved the value of preventive serotherapy, to say nothing of the recent statistics of Sieur and Bazy.

Sieur published in January, 1915, the statistics of tetanus in the army. He had observed 7 cases among 17,507 wounded, or ·039 per cent., and this low

proportion was due to the systematic administration of preventive injections to all the wounded.

Bazy, among 10,986 wounded men in hospitals in the entrenched camp of Paris, reported only 129 cases, and in those sections of the army in which a preventive injection was given to every man wounded, the proportion of tetanic patients was ·48 per cent., while in the other sections it was 1·299 per cent., or three times as high.

Out of 200 wounded men 100, without exception, and without selection, were given preventive injections; only one contracted tetanus. In his case the prophylactic injection was given too late; in reality the morbidity, for this series, was 0. A hundred soldiers subjected to the same conditions, but given no preventive injections, yielded 18 cases of tetanus, or nearly one case in five.

Fifty other wounded men, comprising 10 with wounds in a state of suppuration, produced by shell-splinters, and 40 with wounds produced by rifle-bullets, received each one a preventive injection; not one of them had tetanus. This injection was given within five days of the infliction of the wound.

These figures appear to us the best demonstration of the efficacy of preventive serotherapy, and it would be still more efficacious if, as we shall now explain, physicians did not content themselves with a single injection, and if the requirements of serotherapy were more carefully fulfilled.

Rules of Preventive Serotherapy.—(*a*) As a general rule, every wound received in war should be regarded as contaminated by tetanic spores; just as every wound, large or small, contaminated by the soil or produced by an infected object, calls for a preventive serotherapeutic injection.

While those wounds which are accompanied by extensive laceration or destruction of the tissues, together with complicated fractures, are most liable to be complicated by tetanus, we must not neglect seton-like wounds, or slight and superficial wounds, which are all the more likely to be the starting-point of tetanic infection because many surgeons regard them as unimportant and devoid of gravity.

We will even go so far as to say that in the case of every wound received in war time, whatever its situation, its extent, and the nature of the projectile causing it, the physician should have recourse to an injection of antitetanic serum as a prophylactic measure.

Similarly all accidental wounds, frost-bites or chilblains which have reached the ulcerative stage, or have mortified, and all burns, should be followed by preventive antitetanic serotherapy.

(*b*) The injection should be given *as soon as possible*, before the toxin has had time to diffuse itself through the system ; which it does, by the way, very rapidly. In many cases of tetanus which have developed in spite of a preventive injection, it is found that the injection was administered one, two, or three days after the traumatism.

(*c*) Contrary to the belief current among medical writers in the early days of serotherapy, *a single injection is not sufficient.* We know, in fact, that the period of immunity conferred does not exceed eight days, and that the tetanic bacillus may persist much longer than this. Among the sixty cases reported by Chattet in 1909, it is interesting to note that there were only four cases which developed after two injections (Desplas, Cazin and Leriche), and even in these cases the two injections were given at an interval of twenty-five days.

We have already considered the special development of certain forms of tetanus subsequent to preventive serotherapy, and need not further insist upon it here. Under these conditions tetanus may be local, and its onset insidious and precocious; often, on the other hand, it is late in making its appearance. It follows that in the case of every doubtful wound there is reason to administer a second injection eight days after the first, and that in the case of contused wounds it is advisable to give three or four injections, at eight days' interval. This brief interval between the various injections has the additional advantage of protecting the patient against anaphylactic symptoms. We know, indeed, that these symptoms occur eight to ten days after the first injection, and that their onset assumes the form either of erythema or arthralgia, or respiratory disorders which pulmonary examination fails to justify. It is then that the three orders of symptoms appear which are characteristic of the anaphylactic state, and which, if they occur, should by themselves lead the physician to diagnose anaphylaxis. They are, to recapitulate:

1. Modifications of the pulse. These are variable; acceleration of the pulse is a constant symptom, but sometimes it is not only rapid, but small and irregular, while sometimes it is unequal and intermittent.

2. Modifications of the respiration, which consist of an extraordinary amplitude of the respiratory movements. Sometimes the inspiration alone is prolonged and difficult, expiration taking place suddenly and noisily, and being followed by a very long pause. In certain cases stertor may be noted, or Cheyne-Stokes breathing.

3. Coma completes the clinical picture and con-

stitutes, in association with the modification of the pulse and the temperature, the bulbar syndrome of anaphylaxis. Sometimes this coma makes a sudden appearance; sometimes it is preceded by a period of somnolence, of apathy, of semi-coma. Its appearance, as a rule, follows that of the disorders of the pulse and the respiration. It announces the terminal period.

In addition to the bulbar syndrome, sphincter disorders and convulsions have been reported.

The development of these anaphylactic symptoms may end in death or recovery.

With regard to late-appearing tetanus, if we carefully analyse the observations published by Bérard and Lumière, it seems probable that in many cases inoculation was effected at the moment of the latest surgical intervention. Accordingly, even those patients who have received the two regulation injections shortly after being wounded should be given a fresh dose of antitetanic serum whenever it becomes necessary to resort to surgical intervention, as this may result in the liberation of the septic products latent in a suspect wound. Since Bérard and Lumière have applied this rule they have observed no further cases of late infection.

What is now the dose of serum which should be injected preventively? In France the serum supplied by the Pasteur Institute is employed. Of this at least 10 c.c. should be injected as a dose. Certain physicians increase the amount for the first dose, injecting 15 c.c. or 20 c.c. the first time; others recommend the injection of 10 c.c. daily for the first three days.

If the American serum be employed, the usual dose is again 10 c.c.

Lastly, the prophylactic serum should be administered subcutaneously.

An Adjuvant to the Prophylactic Serum.—Salol.—Certain writers recommend the employment, in addition to the antitoxin, of large doses of salol—4 to 6 grammes daily—as a preventive. Although the effect of this medication is doubtful, the drug may be utilised (being inoffensive), especially if there is a dearth of serum.

Curative Treatment

When the first signs of tetanus appear—trismus and contractures, generalised or localised—it is, of course, too late for prophylactic measures. We must endeavour to cure, or to struggle against, the declared tetanic infection. The treatment, then, must be specific; we must resort either to antitetanic serum or to injections of carbolic acid. At the same time the treatment should be symptomatic, and the clinician must endeavour to find remedies for the accidents of tetanus: contractures, pains, and asphyxia.

Local Treatment.—Before discussing the various methods employed in the treatment of tetanus, it must be remembered that the tetanigenous wound must not be neglected, but must be treated. As in the prophylactic treatment of wounds, it must undergo disinfection, clearing out, and drainage. The usual antiseptics already mentioned will be employed. Insufflations of oxygen may also be employed, with the oxidising agents, oxygenated water, carbolic acid, and light; they are not, as a rule, very effective. It must also be remembered that in some cases amputation results in a mitigation of serious symptoms.

The physician should always search for projectiles; a great improvement has sometimes been observed after

the removal of foreign bodies (usually shell-splinters) on which the tetanic bacillus has been found.

Specific Treatment—Curative Antitetanic Serotherapy.—Certain writers question the curative value of the serum; in any case it is less clear than its preventive action. From their experiments upon animals, Roux and Vaillard had already concluded that antitetanic serum possessed no curative action on declared tetanus. When indeed, the first symptoms make their appearance "the toxin elaborated at the centre of infection has reached the nervous centres, and these may be so far invaded that death inevitably ensues. Certainly the antitoxin injected under the skin or into the peritoneum neutralises the toxin in circulation, but it does not remedy the lesions produced, and can do nothing against an accomplished poisoning" (Vaillard).

The experiments of Nocard have also demonstrated that the serum has no modifying action upon confirmed tetanus. However, when injected into the brain itself (intra-cerebral injection) it may produce a successful result.

Thus Roux and Borrel conceived the idea of bringing the serum directly into contact with the nervous substance, and in guinea-pigs which had been rendered tetanic the intra-cerebral injection of the serum arrested the development of the tetanus, and the animals recovered. We shall presently consider the value of this method in human therapeutics.

Good results may also be obtained by injecting the serum in the neighbourhood of the nervous centres. Thus, parabulbar injections have produced 7 recoveries out of 13 cases in the dog (Camus).

However this may be, if we analyse the various statistics relating to curative serotherapy our judgment

is predominantly favourable ; the curative action of the serum cannot be denied. Thus, according to a first series of statistics, among 190 cases treated without serum the mortality was 79 per cent. ; among 330 cases treated with serum it was only 62·1 per cent.

In a second series of statistics 15 cases treated without serum (an admixture of slight cases and cases *in extremis*) yielded 3 recoveries and 12 deaths ; while 152 cases treated by antitoxin yielded 47 recoveries and 105 deaths.

If we combine the observations recently published by Comby, Massary, Roger, Réals and Thomy, and Étienne, with the table which the last writer published in 1900, we have a manifest proof of the efficacy of serotherapy in declared tetanus. We reproduce Étienne's table ; it is based on the period of incubation.

Incubation	Recoveries	Deaths	Mortality	Mortality before the Introduction of Serotherapy, according to Brunner
1 to 5 days .	3	7	70%	90%
5 to 10 ,, .	20	7	29%	70%
10 to 12 ,, .	7	1	13·3%	...
Over 12 ,, .	15	1	6·6%	...

Haushalter, employing the method of massive injections, has published statistics of 32 cases, in which he was able to determine the length of the incubation period. Although these statistics were obtained under bad conditions, since they refer to men wounded in battle, many of whom were left for several days on the battle-field, or to men taken to hospital while the tetanic paroxysms were at their height, this table (p. 194) is particularly instructive.

In the military hospital at Nancy, L. Spillmann observed a mortality of 50 per cent. in the group of cases for which he was able to employ serum, or 9 deaths and 9 recoveries, 5 of these latter being cases of subacute tetanus and 4 of acute tetanus.

In curative serotherapy the surgeon should :

1. Commence the treatment as early as possible—directly the slightest symptoms make their appearance.

Incubation	Recoveries	Deaths	Mortality
5 days	1	1	
7 ,, ...	...	2	62·5%
8 ,, ...	1	2	
9 ,, ...	1	...	
10 ,, ...	7	8	
11 ,, ...	2	1	43%
12 ,, ...	3	...	
13 ,, ...	1	...	
14 ,, ...	1	...	0
16 ,, ...	2	...	
Or among 33 cases	19	14	42·5%

2. Employ massive doses of serum, without, however, exaggerating them ; we shall return to this point when discussing the various modes of treatment.

Modes of Treatment.—The antitetanic serum may be introduced into the system in several ways, which we shall proceed to describe : under the skin, into the muscles, into the veins, into the arteries, into the spinal cavity, and into the cranial cavity.

Subcutaneous Injections.—Surgeon-General (Médecin-Inspecteur) Chavasse has reported excellent results obtained by the employment of antitetanic serum in subcutaneous injections, the dose being 60 c.c. to 100 c.c., divided into two injections per diem, and repeated for two or three successive days.

According to the majority of clinical writers, 50, 80, or 100 c.c. of serum should be injected the first day, and then 40 to 50 c.c. daily, this being continued for at least eight days. It should be mentioned that this is the method least likely to give rise to seric accidents and anaphylaxis. We shall return to this point later on.

In any case, the intensive doses should be continued as long as the tetanic symptoms persist, but as the quantity of heterogeneous serum injected is not a negligible element, and as anaphylactic accidents occur principally after heavy doses, we think it possible to apply an efficacious serotherapeutic medication without employing such massive doses, for the injection of exaggerated doses may become a danger.

The treatment by subcutaneous injection is regarded by certain foreign writers (Germans) as of illusory value, and they employ it only as an accessory means. They inject the serum in the periphery of the wound, or they introduce the bulk of the serum into the system by intravenous or intralumbar injection, making injections in the region of the wound merely in order to augment the dose thus injected.

Intramuscular Injections.—Recommended by certain writers; this method does not appear to us to be advisable.

Intravenous Injections.—Recommended by José Penna in particular, many clinical writers regard these as constituting the best method of treatment. Intravenous injections should possess the advantage of being more active than subcutaneous injections. Still, it must be remembered that intravenous injections are more liable to provoke anaphylactic shock, and we consider, with Carnot, that their therapeutic superiority is by no means established. We know that in studying

the anaphylactic shock experimentally the liberating dose administered to animals prepared by a previous injection is administered by intravenous injection. The intravenous injection of a very small quantity of serum suffices to cause the immediate appearance of violent symptoms, which closely resemble those which Carnot recorded in his patient, the observation of whose case we have already reproduced in detail. The rapidity and violence of the anaphylactic shock, the hypotension, the cardiac derangement, and the cyanosis are such that we, like Carnot, never give intravenous injections of serum to patients who have already been inoculated, no matter what the date of the previous inoculation. Moreover, it results from the interesting experiments of Jean Camus that while curative antitetanic serotherapy produces visible effects during the course of declared tetanus, the results produced by intravenous injection are in no way superior to those obtained by subcutaneous injection.

Whatever may be the truth of this criticism, the partisans of this method recommend the introduction into the circulation of 100 c.c. of serum at the first injection, this dose being followed by one of 40 c.c.

Walter, Barnsby, and Mercier recommend injections decreasing from 50 c.c. to 10 c.c., associated with intravenous injections of chloral. These authors are said to have obtained 6 recoveries out of 8 cases.

Lemonnier reports a total mortality of 42 per cent., with 8 recoveries out of 19 cases of acute tetanus. Morax, Achard, Castaigne, and Touraine and Francon have obtained successful results. Torrès, in Buenos Aires, reports a mortality of 32 per cent. for 110 cases. He injected 120 c.c. in the first place, and afterwards 100 c.c.

Certain writers recommend that the injections should be warmed, as accidents are said to be avoided if this is done. According to the same writers, by the repetition of injections every two hours an immediate action of the serum may be noted. The general contracture of the muscles is said to be influenced but slightly, or not at all, but the cramps are said to lose visibly in frequency and intensity. Finally, the action of the serum is said to be more rapid than when administered by intralumbar injection.

In this connection, one writer even went so far as to treat a man suffering from a wound in the elbow, inflicted by a shell-splinter, and complicated by tetanus, by means of strong doses of serum, administered by subcutaneous and intravenous injection, which were continued until the appearance of anaphylactic symptoms. The wounded man recovered.

Despite these encouraging data, we think it as well to repeat that for the reasons already given we do not as a general rule recommend intravenous injection.

Intra-arterial Injections.—Heddaus has recommended intra-arterial injections, for the reason that the arterial circulation forms the most direct and efficacious path to the brain. The technical method employed is the following: the carotid artery is laid bare, under either general or local anæthesia, and the needle is plunged into it obliquely in the direction of the blood-current. The serum is thus injected into the blood. In no case have there been disagreeable accidents. The small wound is closed with three or four Michel's clamps.

In France this method of carotid injections has been employed by Gauthier and Chattot. But as we have already remarked, the injection of the serum into the blood-stream does not yield better results in the treat-

ment and cure of tetanus, and we therefore reject it as dangerous and complicated.

Intra-cerebral Injection.—This method, which experimentally is infallible, according to the investigations of Roux and Borrel, has not, with human subjects, given the results which one might have expected from it.

Clinically speaking, failures are numerous, and indeed the rule; moreover, a considerable number of serious and sometimes fatal accidents may occur (delirium, epileptiform convulsions, etc.). It is said that recent statistics have yielded 52 fatal cases out of 84.

Intra-cerebral injection is not at present practised.

Sub-arachnoid Injection.—This method, employed principally abroad, has been recommended in France by Doyen. This surgeon is said to make intra-rachidian injections of 60 c.c. the first day, and 40 c.c. the second day. He makes his patient lie in a bulbar declivity of forty-five degrees, claiming that the serum in this way reaches the nervous centres. He is said to have lost 3 patients out of 24 treated, thus obtaining a death-rate of 12 per cent.

In England Dr John Eyre, of London, and Dr Blair regard intra-rachidian injection as the best method of treating tetanus.

Clinically speaking, it must be remembered that lumbar punctures are very difficult in tetanus patients—even impossible, except under general anæthesia, under chloroform by preference, in order to avoid broncho-pulmonary complications. This intervention becomes a difficult complication in a contractured patient, for whom the most absolute repose is a fundamental necessity. Moreover, the injection may cause a slight inflammation of the serous membrane. Aseptic puriform meningeal reactions (Widal, Sicard and Salin)

are exceptional with French serum. However, when aseptic seric meningitis does result, the symptoms develop in the following order. Three or four hours after the injection, headache makes its appearance, together with a trace of Kernig's sign. The symptoms reach their maximum severity, according to Sicard and Salin, about the fifth or sixth hour, then becoming gradually attenuated and disappearing on the second day. Examination of the cerebro-spinal fluid shows :

1. The presence of polynuclear leucocytes, which are intact, and are not modified as at the commencement of an infectious meningitis.

2. The presence of red corpuscles in abundance.

3. At other times the liquid is found to have changed colour, being thick, opalescent, puriform.

This aseptic serum meningitis is never fatal.

Intra-nervous Injection.—Guided by Mayer and Ramson's experiments upon animals, certain physicians have tried intra-nervous injections, with a view to checking the invasion of the nerves by the toxin. Thus, the case has been reported of a laboratory attendant, who is said to have been saved by an injection of serum in the brachial plexus. These injections are said, moreover, to obviate the amputation of a limb. It is obvious that the introduction of the antitoxin into the nerves is effected more certainly if the brachial plexus is previously laid bare below the clavicle, the sciatic nerve in the bend of the thigh, or the crural nerve in the crease of the groin. In thin subjects this uncovering of the nerve is easy, and the serum may then be injected into it, but this method sometimes aggravates the local tetanus of a wounded extremity. In France two principal methods have been employed of acting upon the nervous trunks which conduct the toxin

from the wound to the medullary and cerebral nervous centres.

These are: the *para-nervous injections* recommended by Sicard, which are made at the root of the limb, in the neighbourhood of the nerves;

The *para-radicular injections* of Apert and Lhermitte, which are administered epidurally in the sacral region. They offer a double advantage: in the first place, they are less difficult to give than the preceding kind, and they surround all the nerve trunks proceeding from the lumbar and the sacral plexus with antitoxin, while the serum is not diluted as it is in the cerebro-spinal fluid. Vautrin, however, has been unable to discover that this method is of any greater efficacy.

Injections of serum *in immediate contact with the wound* have also been recommended. Thus, in four cases, Jousset conceived the idea of administering deep injections of 20 to 30 c.c. of serum about the pharynx, in the submaxillary region. These injections calmed the trismus and the dysphagia.

Of all these methods, one in particular is above all criticism—namely, *the subcutaneous method.* It is not sufficient by itself to cure tetanus, which demands, as we shall see, a combined treatment. And although no one method has proved itself to possess such efficacy as to impose itself above all the rest, we have deemed it of interest to recapitulate the various methods which have been successively employed in curative serotherapy.

Antitoxic Treatment

Treatment by Carbolic Acid (Bacelli's Treatment).—Bacelli, in 1888, advised the subcutaneous injection, in cases of tetanus, of carbolic acid in a 2 or 3 per cent.

solution. The injections should be given several times a day until the tetanus has terminated (twenty days and more), each injection containing ·03 to ·04 gramme of carbolic acid.

The happy results obtained by this treatment might point, according to some writers, to the fact that the cases treated were not severe. By this method at least 1 gramme, and even more, of carbolic acid must be introduced into the system. The injections are not very painful, and are not accompanied by any renal symptoms.

In the majority of cases, about half-an-hour after the first injection, a sedative effect is produced, with a diminution of the contractures. This phenomenon, manifested more particularly in cases of little gravity, is said to be more readily obtained with sulphate of magnesium. Consequently, certain writers consider that the carbolic acid treatment should be reserved for very slight cases.

To avoid any caustic action, certain physicians employ oily solutions (Margliano, Gerest, de Montille, Lesage).

In France this treatment is frequently employed, above all in combination with serotherapy (de Massary, Roullaud, Goumez, Laurent), or alone (Caillaud, Cornoglion, Migay), or in association with chloral (Sainton).

Sainton recommends the following procedure: Twice a day the patient is given an injection of 40 c.c. to 50 c.c. of a 2 per cent. solution of carbolic acid, so that the daily dose varies between 1·6 grammes and 2 grammes. The injection is subcutaneous, and is given, preferably, above the seat of the wound and in its neighbourhood. The injections may be continued for several days, and in the case of two patients Sainton

continued the treatment for nearly a month; and he has, in two cases, introduced 48 grammes of carbolic acid into a patient's system without provoking symptoms of poisoning. The urine, in particular, never exhibited the characteristic black tinge. By this method, in association with chloral (12 to 16 grammes daily in two enemas), Sainton obtained positive results, although in two cases which terminated in recovery the symptoms had assumed a very grave development.

Intravenous and intra-spinal injections have not been much investigated.

Two writers have made experimental investigations with animal subjects, in order to determine whether carbolic acid has a prophylactic action. In mice previously injected with carbolic acid they succeeded in attenuating the tetanic infection, in retarding death, and even in averting it. Carbolic acid, then, should possess prophylactic and not merely curative properties.

Mode of Action of Carbolic Acid.—It is said to act on both the serum and the toxin.

In vitro, it is said to annul the toxic action of a large dose of a culture of tetanic bacilli.

In vivo experiment hardly bears out the hypothesis of action upon the toxin; it does not modify experimental tetanus. At the same time, successful results have been obtained in human tetanus.

Thus, in the case whose particulars were published by Stewart and Laing in *The Lancet*, 26th December 1914, the tetanus became aggravated in spite of large doses of serum, chloral, and bromide; it was cured in a month as a result of the subcutaneous injection of carbolic acid (2 c.c. of a 5 per cent. solution every two hours, under the skin of the abdomen).

Colloidal Metals.—As an antitoxic treatment, the colloidal metals might be employed: collargol, electrargol, lantol, colloidal gold.

Alcohol.—As chemical substances might exert a detrimental action on the antitoxin, alcohol has been suggested and recommended, as it should act as a narcotic.

Dutertre, in this connection, mentions a case of tetanus which he had occasion to observe some twelve years ago in the hospital at Boulogne-sur-Mer. The patient was a vagrant, who, subsequently to a wound in the face, inflicted by a kick, was attacked by tetanus. Some comrades who called to see him secretly brought him a litre of brandy, of which he drank every drop, so that by the evening he was dead drunk.

Next day the patient was better, and a few days later he left, cured. Dutertre compares the result obtained by alcohol in this case with the result obtained in cases of snake-bite. We know that many persons bitten by venomous snakes have made themselves drunk, and have escaped death.

As Dutertre remarks, the arterial tension, being increased by the absorption of a large quantity of alcohol, may perhaps retard the toxin production of the wound. Perhaps, also, the presence of a certain amount of alcohol in the blood annihilates the action of the tetanic toxin.

Salvarsan.—Favourable results have been reported from the employment of salvarsan in cases of tetanus. In the two first cases the employment of salvarsan was associated with the antitoxin treatment; the patients recovered. Of six other patients, two presenting a tetanus of medium severity recovered after the employment of salvarsan.

The four remaining cases of tetanus were of a serious character. Treated by salvarsan, one died of pneumonia; one recovered; the two remaining cases showed great improvement.

The writer who reports these results believes that salvarsan acts favourably upon tetanus. The grave and rapid development of tetanus is said to become milder and slower, and the duration longer. It is possible, says this writer, that salvarsan alone would act in the same way as antitetanic serum.

According to him, the treatment should commence with antitoxin directly tetanus is declared, and salvarsan should be given on the second and perhaps the third day. Two injections of ·05 gramme of salvarsan should suffice.

Other writers have made investigations in order to judge of the value of this treatment, and it must be recognised that a number of cases have not been favourably affected by salvarsan.

The results at present being what they are, we do not advise the employment of this drug in tetanus, whatever the clinical appearance or severity of the disease.

Ascitic Fluid.—The injection of a serous exudate in cases of tetanus might, according to certain writers, lead to an amelioration of the dangerous symptoms. The liquid to be injected is collected in a sterilised flask and injected five to ten minutes later. This serous exudate is rich in lymphoid cells and albumin.

Other Antitoxic Agents.—Among the substances capable of neutralising the toxin *in vitro*, hydrochlorate of betain has been suggested (Jaboulay), and cholesterin. which is said to fix the toxin in the nervous system. Nervous opotherapy has also been recom-

mended, this suggestion being inspired by a mistaken interpretation of the experimental results obtained by Wassermann and Takaki in respect of the neutralisation of the toxin by cerebral pulp.

A. Lumière and Chevrotier have investigated the action of oxidising agents on the tetanic toxin, and their experiments, conducted first *in vitro*, then *in vivo*, with the guinea-pig, dog, goat, and ass, have led them to the conclusion that among the many substances tested the *alkaline persulphates* possess in the highest degree the property of exerting a destructive action on toxins.

Guinea-pigs which are given subcutaneous injections of a solution of *sodium persulphate* some minutes or some hours after the injection of the toxin always survive the experiment. The period of survival varies according to the dose of toxin administered.

Persulphate of sodium, according to Lumière and Chevrotier, exerts a constantly favourable action upon the paroxysms of contracture, alleviating or even suppressing them. The remarkable effect of the persulphates upon the tetanic spasm having been thoroughly verified in man, these writers have employed this method in all their cases of tetanus.

The treatment consists in injecting 20 c.c. of a 5 per cent. solution of pure neutral persulphate of sodium intravenously, once or twice a day, according to the gravity of the infection. These injections may be continued for eight to fifteen days, their frequency being regulated according to the development of the spasmodic symptoms ; they are given at longer intervals when the paroxysms cease, but more frequently if they persist.

The persulphate should be kept protected from

damp, and in the solid state, in sealed tubes containing quantities of 5 grammes. In solution it keeps only for a few days, and the solution is decomposed by heat. It should therefore be prepared as required, by dissolving each dose of 5 grammes in 100 c.c. of cold distilled and sterilised water.

When a solution is not employed within a week it should be thrown away.

The intravenous injection of this drug does not, as a rule, cause any reaction. However, nausea is sometimes observed two or three minutes after the injection, and it may be accompanied by vomiting, which is, however, unimportant.

Immediately after the administration of this medicament the paroxysms, as a rule, cease, or are at least greatly attenuated. The permanent contractures, and notably the trismus, persist without modification. According to Lumière the patients themselves beg for the injections, of which they quickly feel the results. They become, moreover, insensitive to external excitations, and no longer exhibit the afflicting paroxysms which make tetanus one of the most appalling and formidable of diseases.

Bottu's Mixture.—Routier recommends, in addition to the usual treatment with morphine and chloral, which fails in a great many cases, the employment of subcutaneous injections of a saline mixture furnished by M. Bottu.

This saline mixture is composed of pure and very stable persulphate of sodium, and phosphate of calcium sufficiently rich in free phosphoric acid to render the whole soluble in ten parts of water.

This preparation takes the form of a white crystalline powder, odourless, with an acid flavour which keeps

perfectly without giving off oxygen, as do the commercial persulphates of sodium, which are always more or less decomposed, and, moreover, contain an often large proportion of sulphate of ammonium. The mixture contains one-fourth of its weight of phosphoric acid (H_3PO_4). This powder is completely soluble in distilled water, but should not be dissolved until the moment it is required when employed for subcutaneous injections.

In this way small reserves are injected into the system, which, by their slow decomposition, furnish oxygen and phosphoric acid almost continuously.

Subcutaneous injections of Bottu's mixture are given three times daily, the dose being 50 centigrammes of the salt dissolved in 6 c.c. of distilled water. According to Routier a careful watch should be kept on the patient, for in his opinion this treatment predisposes to pulmonary congestion.

These injections are rather painful, but they appear to arrest the pains and contractures. Thus, in the case of the soldier of the 8th Colonial Regiment, observed by Routier, of which we have already given the particulars, the cessation of the injections of Bottu's saline mixture, although the chloral was continued, was followed by the reappearance of the pains and contractures, which ceased when the injections were resumed.

To render these injections less painful, Routier recommends the addition of a third of a Pravaz' syringeful of morphia (1 per cent.) to the saline solution.

Symptomatic Treatment

Hygiene.—Whether the development of the disease is classical or atypical, the hygienic precautions which

such a malady calls for are so well understood that we need not dwell upon them here. We will merely remind the reader that as far as possible each tetanus patient must be isolated in an extremely quiet room, where all causes of excitation are eliminated.

Feeding by the mouth will naturally not be attempted except in those cases where the patient exhibits no contractures of the muscles of the throat, lest the so-called food pneumonia should supervene. Consequently, the majority of tetanus patients, as they suffer from dysphagic disorders, must be nourished by means of nutrient enemas, and in this connection enemas of an aqueous solution containing 7 to 10 per cent. of glucose have been recommended, or injections of serum, or intravenous injections of a 5 or 10 per cent. solution of sugar.

Diuretics are recommended, since it is recognised that the toxins are eliminated by the urine.

Warm Baths.—Tepid or warm baths constitute a means of calming, and according to some writers even of curing slight cases of tetanus, and those of medium severity. The beneficent action of baths, however, has long been noted. Two baths daily are given, the temperature being 97° F. to begin with, increasing to 106°–108° F. The duration of the bath should be twenty to thirty minutes, or at most an hour.

The majority of patients experience great relief from such baths. During the bath there is said to be relaxation of the trismus, an important phenomenon, since bathing would enable the patient to open his mouth more widely, in order to absorb food and medicine.

Care must always be taken of the wounds; they should be protected from contact with the water by impermeable dressings.

Sedative Treatment.—Chloroform.—Martin and Darre and Walter have obtained good results by the employment of inhalations of chloroform in hyper-acute paroxysms.

Ether.—Intravenous injections of 5 to 15 c.c. of ether in 150 to 450 c.c. of normal saline solution (Noël and Souther) cause a profound sleep of several hours after each injection.

According to some writers, ether is said to destroy the combination of the toxin and the nerve-cells.

Potassium bromide, hyoscamus, belladonna, and curare, and, finally, compounds and derivatives of *opium,* may be employed as adjuvants to other sedative treatments.

Morphia, employed in subcutaneous injections of 1 centigramme four to five times per diem, produces repose, and causes the contractures to cease. To this may be added scopolamine, in doses of ·5 milligramme per injection ; the action of morphine, associated with scopolamine, is, according to certain writers, more profound and more prolonged. However, morphia possesses the great defect of causing constipation, cerebral congestion, and respiratory paralysis ; and the patient seems more liable to develop broncho-pneumonia.

Morphia, then, whether associated with scopolamine or not, must be administered prudently. Attempts are sometimes made to replace it by pantopon or paverin.

Chloral.—Chloral is certainly the drug most employed in the course of tetanic paroxysms ; it seems, moreover, to act better than morphine.

Chloral was recommended particularly by Verneuil as a symptomatic medicament in tetanus. By pro-

curing repose and sleep, by causing a cessation of the contractions, it may maintain the strength and prolong life long enough to permit the disease to accomplish its development toward recovery.

There is almost always an immediate and very apparent amelioration; the contractions diminish in intensity and even cease completely. But the symptoms which cease during sleep reappear upon waking, with much the same characteristics as before the administration of the drug (Mathieu). As for definite successes, they amount, according to Verneuil, to two-fifths of the cases treated; this result is certainly exaggerated; but it must be admitted that chloral increases the proportion of recoveries.

It is in chronic tetanus, or rather in the slowly developing form—that is to say, in the atypical forms which we have described—that successful results are most frequently obtained. We shall return to this point when, having described the various therapeutic methods in use, we discuss those which, in our opinion, should by preference be selected for the treatment of the abnormal forms of tetanus.

Chloral may be continued for fifteen or twenty days, and may, as Poncet remarked, lead gently, through prolonged slumber, to convalescence.

Choral is usually administered by the mouth or the rectum.

By the mouth, 1 gramme of chloral is given hourly until sleep and muscular resolution are obtained. This effect, once obtained, it is maintained without interruption, save to feed the patient. He may, in this way, be given as much as 6, 8, 10, 12, 16, or 20 grammes of chloral per diem, and this for several weeks, until the symptoms disappear.

We may, in fact, by commencing with weak doses, very soon contrive to exceed the fatal dose for an adult (this varying between 5 and 10 grammes), but it must be remembered that large doses may produce symptoms of chloralism, which we had perhaps better describe. Nicaise has observed toxic effects with doses of 5 grammes; hence the necessity of avoiding massive doses of more than 3 or 4 grammes.

Chloral poisoning may be acute or chronic.

In the acute form, the phenomena of intoxication betray themselves in dramatic fashion, consisting of profound slumber, abolition of sensibility and the reflexes, and swelling of the face, which is sometimes livid, sometimes red. A more or less œdematous swelling of the conjunctivæ may also be noted occasionally, sometimes with slight ecchymosis, epiphora, and diplopia. At the same time there is either a slow or a weak and rapid pulse, with retardation of the respiratory movements, a contracted, or more rarely a dilated pupil, and coldness of the extremities. The hypothermia may attain 95° or even 91·5° F., and erythematous eruptions may appear, in the form of large red patches, more or less numerous and extensive, urticarial or papular, or by exception purpuric.

Death sometimes occurs suddenly, and is due to the stoppage of the respiration, or more rarely to paralysis of the heart. It may even happen that the patient may succumb when he appears to have recovered.

Gubler divides the syndrome of chloralism into three periods:

1. A phase of excitation, usually but slightly marked, and of short duration.
2. A period of hypnosis.
3. A phase of narcosis or stupor.

Lastly, on awakening, a recurrent delirium may make its appearance (Noir); but the chronic form is that which is usually observed, although this occurs very rarely. It may be mentioned that it is betrayed by:

1. Digestive disorders.
2. Cutaneous eruptions.
3. Disorders of nutrition and respiration.
4. Nervous disorders.

The digestive disorders consist of vomiting.

The eruptions may assume various aspects.

The eruption commences with a diffused redness of the skin, presently followed by a sensation of respiratory oppression, with waves of heat. It may become generalised, but by preference affects the articulations on the side of extension, and the portions of the body chafed by the bed. The patches of eruption, varying in size and form, are usually slightly salient (Aviragnet).

The eruptions may assume any one of five aspects: the erythematous form, the papular form, the urticarial form (Gaucher), the vesical form, and the petechial form. These two last are the least usual.

In benign cases, which are most usual, the eruption disappears very quickly; it gives rise to no febrile reaction or disagreeable subjective sensations. It disappears when the drug is discontinued, leaving no traces behind it; but in those cases in which it is generalised the rash persists for several days, and is accompanied by fever and itching.

The eruptions are more frequent in summer, and are often determined by the ingestion of exciting beverages (coffee, tea, alcohol, etc.).

The disorders of nutrition are betrayed by œdema, ulcerations, petechiæ, or purpura. The patient falls into a condition of considerable weakness, and exhibits

dyspnœa, with precordial anguish or an asphyxial condition.

The nervous disorders consist of insomnia, with agitation, or invincible sleep, weakening of the intelligence, enfeeblement of the senses, tremors, and occasionally epileptiform convulsions or paralysis. The patient usually succumbs while in a state of marasmus, or through enfeeblement and stoppage of the heart, or through paralysis.

In the event of gastric intolerance, or in the case of fully developed paroxysms, the chloral may be administered, as we have said, by the rectum. In this case the irritant qualities of the drug should be allayed by the addition of mucilage, or 120 grammes of milk and the yolk of an egg, making the enema up to 200 grammes. Usually 4 grammes of chloral are given in each enema, and this is repeated, if need be, three to four times a day.

Ore and Mayet have recommended the administration of chloral by intravenous injection, solutions of 1 in 20 or 1 in 30 being employed. This method has not been sufficiently tested to justify its preference over the buccal or rectal administration. However, Mayet reports a case in which, after two intravenous injections of 2 grammes and 1 gramme, separated by an interval of twenty-four hours, a comatose slumber supervened, with irregular pulse and breathing, death occurring three hours after the second injection (*Lyon Med.*, 1891).

To avoid these accidents it is best, according to Mayor, to employ an isotonic solution of a maximum strength of 2 per cent., while care should be taken to give the injection extremely slowly.

It must be remembered, also, that chloral is counter-indicated in heart disease, above all in cases of aortic lesions, *a fortiori* when there is degeneration due to

myocarditis (in alcoholics principally). Chloral is a cardiac poison, and weak doses must therefore always be employed in heart diseases or alcoholism. We have seen that massive doses should be avoided even in the case of adult patients free from any organic defect. If these conditions be scrupulously fulfilled chloral may, according to some writers, be sufficient alone. In certain rare and individual cases it may lead to recovery.

Sulphate of Magnesium[1]

The effect of intra-cerebral injections of magnesium sulphate was studied about nineteen years ago by S. J. Meltzer. He found that after an intra-cerebral injection of a few drops of a 5 per cent. magnesium sulphate solution, the animal turned on one side and remained for hours in a stuporous condition. As a result of investigations extending over the last twelve years with Dr John Auer, Meltzer considers that the dominant action of magnesium salts on the living body, no matter by which way it is administered, consists in depression or inhibition of nervous activity. Consciousness is the first thing which is completely abolished. The unconsciousness is, as a rule, accompanied by a great muscular relaxation, while all the reflexes may still remain nearly unaffected. With a larger dose of magnesium the reflexes, too, begin to disappear, and with a still further increase of the

[1] A somewhat lengthy excursus on the physiological action of magnesium salts has been omitted, and a summary of the views of Meltzer, to whom we are almost entirely indebted for our knowledge of the action of magnesium, is inserted in its place. (*Vide* "Inhibitory Properties of Magnesium Sulphate and their Therapeutic Application in Tetanus," S. J. Meltzer, *Journal American Medical Association*, vol. lxvi., No. 13, March 25, 1916, pp. 931-934.—Ed.)

magnesium dose the motor nerve endings become paralysed—a curare-like action, which is accompanied, of course, by a simultaneous profound central action.

Chemically, calcium and magnesium are closely related substances. Biologically, however, they are strikingly antagonistic to one another. Auer and Meltzer found that an animal which may have been completely paralysed by a magnesium salt can be restored within a fraction of a minute by an intra venous injection of a calcium salt. It must be added, however, that this applies essentially to conditions in which the animal was exposed to the effect of magnesium for a comparatively short time. When the animal is saturated with magnesium for a longer period, the antagonistic action of calcium is less evident and is even not without some danger.

As is well known, the various neurons are not connected by direct continuity but by mere contact. That place of contact is termed by Sherrington "synaptic membrane." The contact between motor nerve and muscle is also not of a very solid character, and is termed by some also synaptic membrane. It is assumed that the magnesium solution contained in the lymph bathing the synaptic membrane enters with ease into these spaces and interrupts the passage of nervous, afferent impulses from one organ to the other, especially of such impulses for which there is a less readily prepared path for transmission than the paths existing for normal active reflexes.

What is said of magnesium applies also to calcium. When it is present in the lymph in a quantity larger than normal, it enters readily into the synaptic membrane and displaces or neutralises the obstructing or inhibiting magnesium.

The effect of magnesium salts was investigated extensively on animals and in a comparatively considerable degree also on human beings by intravenous, intraspinal, intramuscular, and subcutaneous injections. In all modes of administration the effect is, as stated before, unmistakably depressing in character. In intravenous application the effect is rapid, and when so used it must be guarded against possible harmful accidents. The inhibitory effect of an intraspinal injection sets in fairly early, and may last even longer than twenty-four hours. Intramuscular injections have a fairly rapid effect, but its duration is comparatively short. Subcutaneous injections act slowly but have a cumulative effect. Meltzer asserts that no other remedy is capable of relieving the furious symptoms of acute tetanus to such a satisfactory degree as do the injections of magnesium sulphate. On the basis of the above-mentioned theory he states that we may expect from the use of magnesium sulphate perhaps even more than a symptomatic action; it is possible that the magnesium salts, accumulated in the lymph, enter into the synaptic membrane between two neurons, and thus prevent the wandering of the tetanus toxin through higher neurons and into the corresponding nerve-cells.

Influence of Magnesium upon the Temperature of the Body.—Experimentally, in the rabbit, a considerable lowering of the temperature has been noted as produced by sulphate of magnesium. This fall of temperature is not a direct consequence of the narcosis. It is a parallel phenomenon. The magnesium, doubtless, acts directly upon the centre regulating the production of heat. This fall of temperature, moreover, is noted after doses of magnesium which do not produce the slightest

symptoms of paralysis, still less of narcosis. A very careful examination of the thermal curve shows that a very marked parallelism exists between the temperature and the indications of magnesium poisoning. The fall of temperature is proportionate to the rapidity of onset of the symptoms of paralysis and narcosis. With a little practice one may, from the extent and the rapidity of the thermic fall, establish a prognosis of the gravity of the magnesium poisoning.

When narcosis sets in, and also, almost always, when the first symptoms of paralysis appear, these phenomena are immediately announced by a sudden and violent drop in the thermic curve. In the treatment of tetanus, therefore, we must employ sulphate of magnesium with prudence, and must systematically take the patient's temperature; the indications with which it provides us are important guides in the matter of regulating the dose and avoiding accidents.

Action of Magnesium upon the Circulation.—It has long been known that the sulphate and other salts of magnesium are cardiac poisons. Experimentally, it has been proved that magnesium diminishes the blood-pressure without decreasing the frequency of the heart-beats; and that the disorders of the circulation produced by magnesium cannot in any way be ameliorated by calcium. Thus, if we almost kill an animal with too large a dose of magnesium, the respiration disappears and the movements of the heart become less frequent, but an intravenous injection of calcium re-establishes the respiration, while the heart recovers only as the oxygenation of the system becomes improved.

Any therapeutic action of magnesium is accompanied by enfeeblement of the circulation. In the magnesium treatment, therefore, we must pay all the more attention

to the state of the respiration, inasmuch as calcium, used as an antidote, acts only on the respiration, and not at all on the enfeebled circulation.

Mode of Administration and Dose.—Experiments upon the rabbit have enabled us to discover the mechanism of the therapeutic action of magnesium.

Sulphate of magnesium injected under the skin is quickly eliminated.

Its action is in proportion to its degree of concentration.

Experiment has also proved that the rapidity with which magnesium injected under the skin is absorbed is very inconstant, above all when highly concentrated solutions have to be employed.

From these investigations it results that the subcutaneous injection, at one time, of large doses of sulphate of magnesium is, in the treatment of tetanus, an insufficient procedure. It might be advantageous in serious cases of traumatic tetanus, the duration of which is short. In less severe cases, with a chronic tendency, it constitutes only an indication of symptomatic treatment.

Intravenous Injections of Sulphate of Magnesium.—To obtain a rapid and lasting effect, intravenous injections should be employed.

It is possible, with a 3 per cent. solution of sulphate of magnesium in an isotonic solution, to obtain an action of the magnesium upon the terminals of the motor nerves which will last for some hours; an action which is in proportion to the rapidity of injection. By this means we may obtain a condition in which the magnesium, injected into the veins with a certain rapidity, is eliminated by the kidneys with the same rapidity. We may thus, with a given strength of

solution, and according to the rate of injection, affect all the peripheral nerves, while leaving the patient with sufficient powers of respiration, and without producing a notable diminution of the blood-pressure. The action of magnesium injected into the veins may be quickly arrested ; it is enough to remark that experimentally, in animal subjects, its action may be suddenly destroyed by injecting, into a vein, 2 c.c. of a 5 per cent. solution of chloride of calcium. The reaction produced by calcium is of short duration.

In the case of the human subject, therefore, we must pay great attention to the rate of injection, and none but chemically pure sulphate of magnesium must be employed. The commercial salt contains more or less water. (Chemically pure sulphate of magnesium crystallises with about seven molecules of water.)

Simultaneously with its paralysing action, sulphate of magnesium in solution has a very marked diuretic action. The respiration must be watched during injection, and the injection must be discontinued if the respiratory movements become too feeble, or if the patient exhibits cyanosis. In the event of danger an intravenous injection of a 5 per cent. solution of calcium chloride should be slowly administered. This injection will not prevent the action of subsequent doses of magnesium.

Intrarachidian Injection.—This method, recommended by Kocher, is not based on any specific action. In man this method is difficult, and it takes a very long time to inject a single dose. The injection causes a paralysis of the intrarachidian nerve-trunks. The action is more lasting, but the method possesses the drawbacks that we do not know the dosage of the injection, and the exmaination of the respiration during

injection is difficult. Lastly, the action of calcium as an antidote has not been verified; it seems hardly probable.

From experimental researches it follows that:

1. The subcutaneous or even intramuscular injection of a highly concentrated solution of sulphate of magnesium is the worst means of introducing the substance into the system, since we are not certain by such means of obtaining the greatest rapidity of absorption. The paralysing action will be of brief duration, consequently the injection will produce amelioration only in the slighter forms of tetanus.

2. The intravenous injection of sulphate of magnesium has, on the contrary, the advantage of exerting a lasting action on the nerves, and enables us to maintain this action for many hours. It might, therefore, be employed when the patient is in danger of death from asphyxia resulting from cramps. It gives the patient time to recover under the natural treatment of tetanus —that is, treatment by antitoxin. Death from cardiac disorders in tetanus patients results, as a matter of fact, from the intense muscular labour provoked by the cramps.

3. Treatment by intralumbar injections gives results which are longer in duration, and more in proportion to the dose, than those obtained by subcutaneous injection. In a serious case of tetanus intralumbar injection is very difficult, and it cannot readily be often repeated. Moreover, if accidents occur as the result of an overdose their treatment is problematical.

To refer no further to the data derived from experiment, which have thrown some light upon the treatment of tetanus by sulphate of magnesium, let us now consider the clinical results of this treatment.

Two writers have succeeded, by means of the mag-

nesium treatment, under conditions which endangered life, in rendering deglutition and respiration possible, in averting the danger of death during the painful paroxysms, in facilitating alimentation, and in diminishing the number of paroxysms. In one case the number of paroxysms occurring in a given time was thirty-three ; this was reduced to fourteen.

This treatment enables the patient to raise his head and open his mouth, while it dispels the dyspnœa. According to the same writers, sulphate of magnesium injected subcutaneously is an energetic remedy, diminishing the tetanic hyperexcitability and the violence and frequency of the painful paroxysms. It is especially useful in the spasms of deglutition and respiration which endanger the patient's life. It averts extreme weakness and asphyxia ; it diminishes the number and intensity of the cramps. It should not be employed in intrarachidian injections, the duration of which is limited, unless these are clinically necessary. As for technical details, a 20 to 25 per cent. solution should be employed for children and a 40 to 50 per cent. solution for adults. Additional supra-aponeurotic injections should be given, the injection being commenced with a little saline water.

Kocher advises the employment of a 10 to 15 per cent. solution. He injects 5 c.c. of this by intrarachidian, intravenous, or intramuscular injection, and according to this writer intrarachidian and intravenous injections are more dangerous than subcutaneous or intramuscular injections. The results have been encouraging. Kocher claims to have obtained, by this treatment, six recoveries in seven cases of tetanus. Other surgeons, in particular Powers, Miller, Fox, and Johnson, have reported cases of recovery.

Smithson, treating two cases of tetanus by this method, had one death due to paralysis of respiration. In some recent statistics (1914) a writer reports, as a result of bibliographical research, that twenty-seven cases of tetanus thus treated yielded only nine deaths.

How should sulphate of magnesium be employed, and in what doses ?

Subcutaneous Injection.—By this method 10 to 15 c.c. of a 25 per cent. solution of sulphate of magnesium may be injected two to three times a day. This method is said in particular to have yielded excellent results in Monod's hands, as recorded in the observation of atypic tetanus already cited.

It should be remembered that very large doses may be given—as much as 100 c.c. even—and by employing a 40 per cent. solution as much as 60, 80, or 100 c.c. has been injected during the twenty-four hours in extremely serious cases.

Subcutaneous injection of sulphate of magnesium is really painful, and it is often necessary to give an injection of morphia before administering the magnesium.

The effect of the magnesium usually becomes visible after the lapse of half-an-hour, and lasts five or six hours. Under certain conditions the effect may last longer. After the injection the patient falls into a light sleep ; the contractures and muscular cramps are greatly diminished. In slight cases and cases of medium severity these symptoms may even disappear completely.

Sulphate of magnesium injected under the skin has, then, a manifest sedative action, which establishes itself slowly and lasts for some time.

A great drawback is the great pain caused by sub-

cutaneous injection. This pain persists long after the injection, and an abscess may often be observed to develop at the point of injection, which, however, as a rule, quickly disperses after incision. This abscess is caused by a slight hæmorrhage which invades the cellular tissue and the muscles around the point of injection.

Pain, and occasionally necrosis, are two complications which have caused the majority of physicians to abandon the employment of subcutaneous injections in the symptomatic treatment of tetanus by sulphate of magnesium.

However, the statistics are encouraging; certain writers speak of 50 per cent. of recoveries; others are less optimistic; one foreign writer in particular is said to have obtained five recoveries and twelve deaths by this method.

Intrarachidian Injection.—By this method 2 c.c. of a 25 per cent. solution may be injected without accidents.

Griffon and Lian employ a solution of this strength, injecting 1 c.c. for every 25 lb. of the patient's weight.

Ramon and Dury inject 5 c.c. of a 25 per cent. solution. Kocher prefers 10 c.c. of a 10 per cent. solution. Other writers inject 6 to 8 c.c. of a similar solution. In most cases the sulphate of magnesium is observed to act effectually upon the contractures, but as Kocher has stated (who cured four patients out of five by this method), a sudden arrest of respiration may supervene. In one case this writer was even forced to resort to tracheotomy and artificial respiration.

Other writers, to obviate this danger, have advised the intravenous injection of chloride of calcium, or the lavage of the lumbar sac with a saline solution. It is also said that the respiratory disorders are amended by

withdrawing cerebro-spinal fluid and an injection of 1 milligramme of atropine.

It must also be remembered that intrarachidian injections of sulphate of magnesium may give rise to a sudden rise of temperature, cephalea, erythema, zona, retention of urine, paralysis of the lower limbs, coma, and sometimes an intense meningeal reaction. All these inconveniences are perhaps due to impurities in the sulphate.

According to Bienfait and Leroy, who have published three observations, this method enables the physician to gain time, and the employment of an isotonic solution should obviate accidents.

The observations published by Sicard and Drevet and Debre clearly demonstrate the favourable influence of sulphate of magnesium on the painful paroxysms, and afford proof that sulphate of magnesium must be regarded purely as a symptomatic remedy, since death has supervened despite the cessation of the contractures.

Intravenous Injection.—In this method a 3 per cent. solution is usually employed. There are two difficulties to be avoided :

1. The solution should not be too dilute, or the circulation would be needlessly disturbed.

2. Neither must the solution be too concentrated, or it would cause osmotic disorders in the blood and tissues.

Intravenous injections of sulphate of magnesium have not been very largely employed in France. It does not seem that intravenous injection offers any advantages over intrarachidian or subcutaneous injection.

We mention it only for the sake of completeness in

this summary of the different treatments at present employed in combating the tetanic infection.

Symptomatic Surgical Treatment.—In the event of the grave asphyxial phenomena which result from the contractures of the respiratory muscles, certain writers have advised tracheotomy, and others phrenicotomy.

Tracheotomy.—One writer, in two cases of severe tetanus, with imminent danger of death as a result of cramps of the respiratory muscles, performed tracheotomy. The improvement in the respiration was surprising; the cyanosis disappeared almost entirely during all the paroxysms subsequent to the operation. It seems as though the occasional sudden death of tetanus patients in these cases is due, not to the cramps of the diaphragm and other muscles of the thorax, but rather to the trismus and the contracture of the muscles of the tongue, pharynx, and larynx.

Bilateral Phrenicotomy.—Jehn, of Zurich, has advised bilateral section of the phrenic nerves in the dangerous contractures of the respiratory muscles provoked by tetanus.

In these serious cases the diaphragm remains convulsively contracted in the position of maximum inspiration. The intercostal muscles and those of the neck and thorax are themselves contractured. They accordingly hold the thoracic cage immobilised in the position of forced inspiration. Active or reflex movements of the diaphragm and the ribs are consequently impossible, hence the impossibility of changing the volume of the pulmonary apparatus, the cessation of respiratory exchanges, and the imminence of asphyxia.

These mechanical reasons are a complete obstacle to artificial respiration. The thorax has lost all power of movement; the contractured diaphragm bounds it

below, while the osseous portion above the diaphragm becomes a sort of box, with rigid walls, imprisoning the lungs.

In these cases narcotics act too slowly. General anæsthesia cannot be attempted. Artificial respiration fails absolutely in these cases of tetanic cramps. As for sulphate of magnesium, the dose is too uncertain, and its action is transitory. Lastly, a simple or double pneumothorax, which has the advantage of liberating the lung, permits of the re-establishment of the intra-pulmonary exchanges by artificial inspiration and expiration, but artificial respiration must be continued until the cessation of the paroxysm, and the grievous consequences of such respiration are well known.

Phrenicotomy completely paralyses the muscles of respiration, and the augmentation of the intrabronchial pressure, followed by a diminution of this pressure, gives rise to pulmonary movements.

Experimentally we know that the bilateral section of the phrenic nerve in an animal involves no disorders. Basing his argument on this fact, Jehn, in a case of tetanus with dangerous respiratory cramps, proposed bilateral phrenicotomy. Artificial respiration was found to be possible after the operation, and he was thus able to calm thirty-five grave attacks of asphyxia. But this paralysis of the diaphragm must not be resorted to except to permit of artificial respiration.

From Jehn's observation it results that the bilateral section of the phrenic nerves involves no danger, cardiac or other, and this paralysis of the diaphragm does not prevent expectoration. There is one fact which must be remembered—namely, that Jehn's patient was able to draw in only a small quantity of air

at each inspiration; but clinical observation proves that the respiratory exchanges may be very greatly diminished without the production of marked organic disturbances. The organism, as a general thing, adapts itself to all such modifications.

Still, if we take into account the frequency of broncho-pneumonia in cases of tetanus it seems that we should have recourse to phrenicotomy only in desperate cases with grave and acute asphyxia.

Conclusions

Mixed Treatment.—Now that we have described the various therapeutic methods successively recommended in tetanus, whatever its clinical development, we propose to conclude this chapter on the treatment of atypical tetanus by summarising the procedure which appears to us the best and wisest to follow when the clinician is confronted by an abnormal form of tetanus.

It is enough to recall the pathogenesis and development of the tetanic infection. In the infected wound the bacillus of Nicolaïer, favoured by saprogenous associations, secretes its toxin, which may, as the investigations of A. Marie have established, follow the course of the nerves until it reaches the medullary and bulbar centres, where it fixes itself, or may be transported by the circulation.

From this moment the infection is completed, and, as Sahli has clearly demonstrated, the nervous cells modified by the toxin react for a certain time on their own account—thus creating the tetanic syndrome. So true is this that the cellular reactions, with the contractures which are their symptoms, may continue to manifest themselves, may develop, and may determine

a fatal result when the toxins have been eliminated from the system.

In the development of tetanus, then, we may recognise three phases :

1. The bacillus secretes its toxins ; this is the phase of infection.

2. The toxins invade and fix themselves upon the nervous cells ; this is the period of intoxication.

3. The intoxicated nervous cells cause contracture ; this is the phase of cellular reaction.

As Étienne has justly remarked, there is every reason for believing that these different phases overlap in the clinical picture. It is possible that those nervous cells which are attacked by the toxin may be disintoxicated by antitetanic serum, at all events when their progressive impregnation has not given rise to irremediable lesions. They may become disintoxicated spontaneously, for contractures may yield where serotherapy has not been employed ; but the serum possibly exerts a disintoxicating action upon them. Such a disintoxication would occur in successive stages, and, as a rule, those cells which are first reached by the toxin—that is, those whose impregnation is elective—would be the last to become disintoxicated. Thus the trismus, which is the first clinical manifestation in the classic or cephalic forms of tetanus, is often the last tetanic symptom to yield to serotherapy.

On the whole, tetanus may be regarded as an infectious malady, as an intoxication, and finally a nervous malady ; the necessity of a mixed or combined treatment will accordingly be perceived.

A special treatment corresponds to each of the three phases of tetanic development : to the first phase corresponds the suppression of the infected centre ; to

the second, serotherapy ; to the third, the symptomatic treatment.

By combining these three treatments we neutralise the invading toxin, the object of the symptomatic antispasmodic treatment being to limit the reaction of the intoxicated cell upon excitation, while the local treatment of the wound aims at suppressing the spot where the toxins are produced.

It will be understood from this that an isolated treatment of incontestable value, such as serotherapy, is not in itself sufficient.

In dealing with a case of atypical tetanus we must therefore :

1. Disinfect the wound, where the toxins are produced. In this connection we refer the reader to the local treatment of tetanus, which we have already discussed.

2. Although localised, the atypical forms must not be neglected. Despite their benign development and occasionally prolonged incubation, they must, from the first symptoms, be treated as energetically and intensively as the normal forms. Finally, it must be remembered that these are the cases which are most susceptible of cure by massive doses of serum. But here we had best repeat that there is no excuse for exaggerating intensive doses, for they do not indefinitely increase the curative effect of the serum.

Moreover, the quantity of serum injected is by no means a negligible factor in the production of anaphylactic accidents, and if they may break out after small injections, they are far more liable to occur after heavy doses. Doses of 100 c.c. seem to us excessive, and by injecting a first dose of 50 c.c. and progressively diminishing it by 10 c.c. each day we doubtless obtain

equally good results. By this method, moreover, Barnsby and Mercier have obtained excellent results.

We ought also to mention, although we do not share his opinion, that Fricker recommends, in the atypical forms of tetanus, small injections of antitetanic serum (5 c.c.) repeated daily. According to this writer this is the treatment which best succeeds in these partial cases.

Subcutaneous injections alone must be employed, and even so the to-day well-known anti-anaphylactic precautions should be taken in order to avoid the appearance of serious accidents.

Heavy doses will never be administered straightway to patients who have received a preventive injection or injections. One should commence by injecting a small dose (·5 c.c. to 1 c.c.), and a few hours later the rest of the dose. The injection should be strictly subcutaneous and not intramuscular, the latter being more anaphylactic. In no case, however, must the fear of anaphylactic accidents prevent the employment of a treatment which may be efficacious ; all that is needful is to give none but subcutaneous injections and reasonable curative doses.

3. Lastly, with the serotherapic treatment we must associate a symptomatic treatment which is all the more to be recommended in the partial atypical forms of tetanus.

Chloral, in doses of 8 to 10 grammes ; carbolic acid, in doses of ·80 to 1 gramme ; subcutaneous injections of sulphate of magnesium (Monod)—these may exert a favourable and curative effect. It has even been claimed that symptomatic treatment has by itself led to recovery in certain partial forms of tetanus. It certainly seems that in these cases there was rather a

question of painful contractures in a wounded subject than of veritable localised tetanus. Bazy and Vaillard have justly remarked that in many cases bacteriological examination and experimental inoculation have failed to confirm the tetanic nature of the affection. One supposes, therefore, that a symptomatic therapeutics may have sufficed to work a cure in cases to which the name of tetanus has been wrongly applied.

Following these hints, despite the too sweeping assertion of Charles Laurent, the clinician may ensure for his patient the conditions most likely to lead to recovery. By the combination of the various therapeutic methods we believe that the mortality in cases of atypical tetanus can be still further reduced. However this may be, localised tetanus remains a serious complication of the wounds received in time of war, so that it is impossible to insist too strongly on the necessity of prophylactic treatment.

We can, without a doubt, diminish the number of cases of tetanus, whatever the variety:

1. By mechanically cleansing, and making antiseptic, all wounds contaminated by the soil or by suspect foreign bodies, immediately, or as soon as possible, after the infliction of the wound.

2. By injecting antitetanic serum preventively in all cases of septic wounds. A first injection should be given immediately after the traumatism, and a second eight days later. If tetanus is exceptional after a first injection, it is excessively rare after a second. We know, indeed, that after these preventive injections immunisation is not always perfect. Very exceptionally it is insufficient, permitting of an eventual outbreak of tetanus. But the residual immunisation has at least this advantage, in these very rare cases, of

localising the infection; and the malady being localised, it develops with a benign prognosis.

3. A fresh injection should also be given before any subsequent surgical intervention, and then the wounded man, in the vast majority of cases, will be safe from any tetanic complication.

SUMMARY OF THE FORMS OF TETANUS

CLASSICAL FORM

Incidence.—Since the introduction of preventive serotherapy, less frequent than formerly. Statistics relating to present war show that frequency may vary from 11·8 per 1000 (Bazy) to ·1 per 1000 (Vallette).

Symptomatology.—A usually brief prodromal period is observed in four-fifths of the cases, and is characterised by *neuralgic pains* in the vicinity of the wound, and dull or shooting or sometimes fulgurant pains along the course of the nerves in its neighbourhood, with spasms, stiffness, and slight and transitory contractures of the various muscles of the wounded area. The subject is next attacked by *trismus*. Then the neck muscles become stiff; dysphagia appears; the facial muscles are affected, causing *risus sardonicus*. The body is arched—*opisthotonos*.

The muscles of the abdomen become contractured, then those of the limb. The entire body now becomes completely rigid.

The contractures are usually intermittent, but recur on the slightest movement or stimulation. Occasionally contracture is localised to trismus without generalisation.

High fever—104° F. up to even 107·5° F.

Often there is retention of urine.

Lastly, the respiratory muscles are affected and the patient succumbs to asphyxia.

Sometimes emprosthotonos, pleurothotonos, or orthotonos replace the opisthotonos.

Diagnosis.—Easy when symptoms are complete. (1) If trismus is the only sign at outset eliminate. Mental affections and angina.

(2) Acute strychnine poisoning gives rise to similar symptoms.

Prognosis.—Grave. Mortality despite serotherapy is still high. Recent statistics show a death-rate amounting to 64 per cent.

ABNORMAL FORMS

A. Sphlancnic Tetanus

Incidence.—Very rare. It occurs in man quite exceptionally after abdominal operations or uterine wounds.

Symptomatology.—Long incubation. Short duration of the malady.

Non-generalisation of the contractures which involve the muscles of deglutition and respiration.

Dyspnœa is marked and always alarming.

Diagnosis.—Eliminate hydrophobia.

Prognosis.—Always fatal.

B. Cephalic Tetanus

(1) *Non-paralytic Type*

Incidence.—Very rare. No signs of facial paralysis. Always wound of head.

Symptomatology. (*a*) Simple cephalic tetanus. Trismus only with contraction of certain face muscles.

(*b*) Dysphagic form. Pharyngeal spasms rendering

alimentation difficult. Sometimes respiratory muscles affected.

(*c*) Hydrophobic form. Violent convulsive spasms, starting in wound, radiating to muscles of neck, face, and pharynx, finally reaching the diaphragm, to cause grave respiratory disturbance.

Diagnosis.—Eliminate true hydrophobia in types (*b*) and (*c*).

Prognosis.—Type (*a*) grave. Still more gloomy if respiratory disorders appear.

In the dysphagic and hydrophobic forms nearly always fatal.

(2) *Paralytic Type*

Incidence.—Rare. Follows a wound of head in the region innervated by the trigeminal.

Symptomatology.—Facial paralysis with contractures localised principally in the cephalic region, above all in the facial region, but the tetanus may slowly invade other regions.

Facial paralysis may precede, follow, or accompany the contractures. It is usually unilateral, occurring on the same side as the wound. If the wound is median, there may be facial diplegia. The paralysis may be partial or complete.

Complete facial paralysis affects the whole seventh nerve, and may cause hyperacusis and disorders of taste.

Partial facial paralysis may involve either the upper or lower branches of the facial nerve.

Diagnosis.—Eliminate (1) direct traumatism involving the facial nerve; (2) hysteria; (3) tic douloureux; (4) traumatic reflex spasms.

Prognosis.—Less gloomy than in usual forms of

tetanus. Mortality in France does not exceed 50 per cent. The facial paralysis usually disappears without leaving permanent traces when the patient recovers from the tetanus.

(3) *With Paralysis of the Motor Nerves of the Eye*

Incidence. — Comparatively rare. Occurs when tetanus follows trauma of the eye and adjacent parts.

Symptomatology.—Occasionally ocular paralysis is earliest manifestation.

The third nerve is always involved; the fourth and sixth may be paralysed also.

Ptosis, strabismus, and a more or less complete paralysis of the external muscles of the eye are the ordinary symptoms.

The internal muscles of the eye may be affected also.

This form may coexist with facial paralysis.

Diagnosis.—Eliminate (1) ocular spasms; (2) cerebro-spinal meningitis; (3) tubercular meningitis; (4) fracture of the orbit; (5) fracture of the base of the skull.

Prognosis.—Cases of ophthalmoplegic tetanus have been fatal. Chronicity is in favour of recovery. The prognosis of the ocular paralysis *per se* is good. In only one case did the ophthalmoplegia last three months.

(4) *With Paralysis of the Hypoglossal (Rare)*

Symptomatology. — Syndrome of labio-glosso-laryngeal paralysis.

C. Unilateral Tetanus

Incidence.—Existence debated. In any case, exceedingly rare.

Symptomatology.—In general the symptoms are for some time confined to one side of the body, and are still predominant there during generalisation, giving rise to pleurothotonos.

Diagnosis.—Eliminate irritative cortical lesion.

Prognosis.—That of classical form of tetanus.

D. Tetanus of the Limbs

(1) *Monoplegic Form*

Incidence.—Rare. But observations more frequent since first case published by Courtellement.

Symptomatology.—The first symptoms consist of a slight stiffness either of the muscles of the wounded limb or the masseters. The onset may be early or late. The first signs are usually pain in the wounded limb, soon followed by a localised contracture. Clonic movements occurring in paroxysms may first appear, followed by tonic contracture, or the contracture may be the first symptom, the limb feeling, on palpation, like a mass of wood.

Sometimes there is slight transitory trismus. There is little or no stiffness of the neck.

There is often a more or less marked contracture of the abdominal muscles.

There is little fever. Temperature is about 100·5° to 101·5° F.

The pulse is moderately rapid—100 to 120 per minute. Not irregular.

The facial expression is anxious.

There is constant exaggeration of the deep reflexes, often with ankle and patellar clonus and hyper-excitability of muscles and nerves under electrical stimulation.

Diagnosis.—Eliminate (1) spasmodic monoplegia due to cerebral or medullary lesion ; (2) irritation of motor and mixed nerves ; (3) contractures due to lesions of bones and joints ; (4) tetany ; (5) hysterical contracture.

Prognosis.—If development be chronic, there is a tendency toward recovery. The prognosis is, however, grave, on account of possible complications or secondary generalisation.

Routier observed six cases with three deaths. Nevertheless, it often tends toward recovery, except in cases of late post-operative tetanus.

(2) *Paraplegic Form*

Incidence.—Rare.

Symptomatology.—According to the seat of the contractures one may distinguish :

(*a*) Superior paraplegic form. Upper arm, forearm and hands forcibly flexed.

(*b*) Inferior paraplegic form. Limbs in forced extension. Foot in position of talipes equinus. Lower leg extended from the thigh, the patella strongly immobilised. The thigh extended at the pelvis. The whole limb hard, as if petrified.

Diagnosis.—Eliminate tetany, hysterical paraplegia, lesion of cord.

Prognosis.—Favourable. Recovery the rule.

E. Localised Tetanus—Abdominal Thoracic Type (One Case)

Symptomatology.—Tetanus confined to the abdomino-thoracic muscles. Not affecting other groups of muscles except masseters, which are slightly affected.

F. Attenuated Tetanus developing slowly after a prolonged Incubation (Very Rare)

Symptomatology.—The first symptoms consist of a slight stiffness, either of the muscles of the wounded limb or the masseters. The facial expression is abnormal.

The general condition remains excellent, and the patient is able to walk. Muscular hypertonia without paroxysmal contractions.

Temperature normal.

Exaggeration of the deep reflexes and excessive excitability of the muscles and nerves to electrical stimulation.

Diagnosis.—Eliminate hysterical conditions.

Prognosis.—Good.

TETANUS

Tetanus represents a widely distributed wound infection, especially in the Western theatre of war, on account of the contamination of the French and Flemish soil with tetanus bacilli and the strenuous fighting in wet inclement weather. A recent analysis offered by Sir Wm. B. Leishman and A. B. Smallman (Lancet, I, 1917, p. 131) is based upon 160 cases which occurred in hospitals in France between July 1st and October 31st, 1916. Of these cases 118 died and 42 recovered, a case mortality of 73.7 per cent. In a preceding group of cases examined in the spring of 1915 the case-mortality amounted to 78.2 per cent. The high death rate in France is due to the ease with which the infection occurs in patients too seriously wounded for transportation to home hospitals in England, and to the relative frequency of gas gangrene and sepsis superadded to the tetanus. Of 351 cases reported by German observers, 242 died and 109 recovered, equalling a mortality of 70 per cent; in the beginning, nearly all the patients died, the mortality later on dropping to about 65 per cent. The onset of the disease was essentially lessened through prophylactic inoculations with tetanus antitoxin, even after very grave shell and shrapnel injuries, otherwise a fruitful source of tetanus infection. Prophylactic injection of protective serum is a routine measure at the front.

Tetanus has been repeatedly known to follow on prolonged exposure of wounded soldiers to cold and wet. In the current war, soldiers with frost-bitten feet have often become the victims of hyperacute, so-called splanchnic tetanus. As pointed out by Vincent (La Presse Médicale, 1 Nov., 1917, p. 632), the soaking of the men's feet for hours in the chilly water of the trenches ultimately leads to oedema and trophic disturbances. The spores of the tetanus bacillus find an entrance avenue in the existing small erosions of the foot. The activity of the leucocytes is inhibited by cold below 15°, which renders them unable to take up the spores. The surviving tetanus bacilli flourish in the oedematous fluid when the limb becomes warm, and the final absorption of this poisonous oedema is equivalent to an injection of tetanus toxin. Acute symptoms may therefore supervene in spite of the serviceable protective injections of antitetanic serum. The skin and the subjacent tissues remain infiltrated and oedematous for several days. The retarded circulation possibly accounts for the difficult access of the antitetanic serum to the imperfectly irrigated territory. The oedema and, therefore, also the onset of tetanus infection are favored by constricting foot- and leg-gear, which shrinks under the influence of moisture. The wearing of large well-greased shoes and woolen socks impregnated with formol ointment is therefore recommended as a precautionary measure.

The quotation of the following summary, given by Dr. Leon H. Cornwall at the end of his paper on war tetanus—published by permission of the Surgeon General; New York Med. J., Oct. 27, 1917, p. 773—conveys in condensed form the present status of knowledge

in regard to the incidence, management, and prevention of this wound infection:

1. Tetanus is a common scourge of war.

2. In the present war there have been more cases of tetanus per 1,000 than in any previous war.

3. Tetanus develops after wounds contaminated by dirt and clothing, and is more frequent after wounds of the extremities than those of other regions.

4. The usual incubation period is from six to sixteen days, but in tardy tetanus may be prolonged to three months.

5. Low temperature and free access of oxygen prolong the period of incubation.

6. The onset is frequently so insidious as to render early diagnosis difficult.

7. The pathway of the infection is along the perineural lymph channels to the spinal cord.

8. Early prophylactic injection of antitoxin should be given in every wound contaminated by dirt or particles of clothing.

9. For therapeutic purposes the serum should be given subcutaneously, intravenously, intraspinally, and endoneurally.

10. To prevent the muscular fatigue due to spasms and convulsions, sedatives are of great value, and absolute rest is of paramount importance.

11. So-called tardy tetanus may occur as late as three months after injury, and is especially likely to follow secondary surgical operations or other trauma at or near wounds previously infected with tetanus bacilli.

12. The prognosis is grave when the disease develops early, but late cases have a favorable prognosis.

Treatment.—The treatment, as mentioned by Cornwall, consists of three varieties: General, local, and

regiminal. The general treatment consists of the use of antitoxin and drugs. Locally, the treatment includes the use of antitoxin for its neutralizing effect, antiseptic surgical care, and the injection of medication with bacterial action, such as phenol and peroxide. Absolute quiet comprises the major part of the regimen.

"For the administration of antitoxin four methods are employed: subcutaneous, intravenous, intraspinal, and endoneural. In every wound contaminated by dirt or pieces of clothing, and especially wounds of the extremities, a prophylactic injection of 1,000 to 2,000 units should be given subcutaneously at or near the site of injury. The value of the local injection of antitoxin in prophylaxis is due to the fact that it prevents the absorption of the tetanus toxin from the wound by combining with and neutralizing it. If, however, the toxin has been absorbed by the nervous system, this method is of no avail. One initial prophylactic dose is not sufficient but should be repeated weekly for three doses or until the wound is healed. After the development of symptoms the subcutaneous method alone is insufficient. It is imperative at this stage to combine with it one or more of the other methods: intravenous, intraspinal, or endoneural. For therapeutic purposes an intraspinal injection of 3,000 to 5,000 units should be combined with 10,000 units intravenously at the same time. The intraspinal dose should be repeated daily until the symptoms subside, and Nicoll (Jour. Am. Med. Assoc., 1915, LXV, No. 24, p. 1983) advises 10,000 units subcutaneously on the third or fourth day."

The alternative channels of administration of the antitoxin are placed by Leishman and Stillman (loc. cit.) in the following order of merit: Intramuscular, subcutaneous, intrathecal, and intravenous. They have a

decided impression that the intrathecal route may be a dangerous one: and think, on grounds both of theory and observation, that the subcutaneous and intramuscular routes might be promoted to a more dignified position than as merely supplementary to the other routes. In their experience with a series of cases, the results of these two methods of introducing antitoxin were better than those of either the intrathecal or the intravenous methods. Should the wound be a single one, and especially if it is on a limb, they believe it would be sound practice to introduce antitoxin, both subcutaneously and intramuscularly, somewhere astride the path which the toxin must travel on its way to the spinal cord. "To do this effectually it would appear, if our ideas are correct, better to divide the dose and inject portions on each surface of the limb and also at different depths amid the muscles. Somewhere among these tissues we know the nerves run along which the poison is traveling, and the more evenly distributed our antitoxin the better would appear the chance that it may attain effective contact with the toxin and achieve our object."

The value of intramuscular administration of tetanus antitoxin has been widely questioned and a number of writers have protested against this recommendation. The British War Office Committee for the study of tetanus in its Memorandum, published in November, 1916, distinctly states that in a case of tetanus the first thing to do is to give an intrathecal injection of antitoxin, as this route is the most valuable.

Amputation of badly shattered extremities is sometimes the wisest procedure, in order to restrict the continued absorption of toxins and thereby improve the patient's prospects of recovery.

General Treatment of Tetanus Patients.—In order to guard against reflex irritation, these patients should be kept in a dark and quiet room, as free as possible from disturbances of all kinds. They should be carefully nourished with liquid foods, as they are usually unable to swallow or chew solid morsels. Rectal feeding or gavage are sometimes necessary. The more rest and sleep the patient can secure the better his prospects of recovery. Sedative drugs, such as bromides and chloral, are often of use for the relaxation of the spasm and the relief of the general restlessness.

Ultra Violet Light.—The spores of the tetanus bacillus are extremely susceptible to the action of ultra violet light, and in civil practice the radiation of infected wounds with the quart lamp has been known to result in the total destruction of the tetanus bacilli. Radiotherapy is a useful supplement to other curative procedures, but the careful surgical cleansing of the wound must never be neglected, on account of the abundant toxin contents of the infectious focus.

Curare has recently been recommended in the treatment of tetanus, as counteracting one of the most dangerous complications, namely, spasm of the respiratory muscles.

Magnesium Sulphate.—In the treatment of tetanus, magnesium sulphate has been successfully employed, both subcutaneously and in intraspinal injections. It acts as an anæsthetic and induces muscular relaxation. The dose is 15 to 20 c.c. of a 20 per cent solution, or 12 to 16 c.c. of a 25 per cent solution, three times daily. Phenol and hydrogen peroxide have occasionally proved successful in subcutaneous and local application to the wound. Oxidizing agents such as potassium permanganate, chlorin water and iodin solution exert

an inhibitory action on the anærobic growth of the tetanus bacillus.

Sodium Persulphate.—Dr. Leyva, on the basis of some personal observations in the American Ambulance Hospital in Paris (Surg. Gyn. Obs., Dec., 1917, p. 613), finds that sodium persulphate combined with the antitetanic serum relieves the pains and spasmodic attacks to such an extent that the patient begs to be given the injections. The minimum dose must be 60 c.c. in one day. The solution must be freshly prepared and kept in a shaded place, as both heat and light decompose it. In the American Ambulance Hospital the solution was prepared in doubly distilled water, using the persulphate of sodium in sealed bottles prepared by the firm Lumière of Paris.

In the management of wound infection by the tetanus bacillus, antitetanic serum has been found to be a defensive measure of the first rank, not only protective, but curative, and absolutely indicated in all cases. In the presence of established tetanus, even when the preventive injection has been neglected, excellent results may be anticipated from its use in sufficient dosage and suitable administration, preferably by the intraspinal route. Tetanus developing in spite of a preventive injection is very amenable to serum treatment, and the patients are almost without exception saved by intraspinal administration of graded doses of antitoxin.

[Editorial Note.]

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SECTION V

MALARIA

MALARIA IN MACEDONIA

Chapter I

PARASITOLOGY

Malaria is due to the development in the organism of a protozoon discovered by Laveran, which is inoculated by the bite of the Anopheles mosquito, and by the female Anopheles exclusively. This protozoon assumes three very different types, which most parasitologists consider nowadays as three distinct species, the *Plasmodium vivax*, the agent of benign tertian; the *Plasmodium malariæ*, the agent of quartan fever; and the *Plasmodium præcox* or *falciparum*, the agent of tropical fever, æstivo-autumnal fever or malignant tertian.

Although they form distinct species, these three parasites should be grouped together under the generic name of malarial hæmatozoa, because they present similar biological and developmental characters and pathogenic properties, and are affected by the same therapeutical agent, quinine. They can only be inoculated into man by the bite of the female Anopheles, in whose organism they undergo an identical evolution; after being introduced by the saliva of the mosquito they reach and penetrate the red corpuscles and develop in the form of a small amœba, which is first of all round (schizont) and then irregular owing to the

pseudopodia protruded from its protoplasm (amœboid body). They increase in size at the expense of the corpuscle which they have invaded. After some time the parasite divides by repeated segmentation of its nucleolus; it then forms a rounded mass, in the centre of which is a collection of pigment, constituted by the union of ten, twelve, or sixteen nucleoli, arranged like rosettes round the centre and each surrounded by a thin zone of protoplasm (*rosette body*). This process of division of the parasites is called *schizogony*. When the rosette body is mature it becomes dissociated. Each of the nucleated elements which constituted it, after being set free by the rupture of the red corpuscle, is discharged as a *merozoite* into the circulating blood, where it fastens upon a red corpuscle, becomes transformed in turn into a schizont, as a merozoite attached to a red corpuscle is called, then into an amœboid body, and finally into a rosette body, the cycle continuing in the same way.

The hæmatozoon also gives rise to certain elements, whose role is all important, known as *gametes* (sexual forms). These elements are formed at the expense of the schizonts and amœboid bodies, which instead of dividing into *rosette bodies* become transformed into a body which is either rounded (in *Plasmodium vivax* and *Plasmodium malariæ*) or falciform (in *Plasmodium falciparum*), and is soon set free in the circulation. This body, which is the *gamete*, possesses two extremely important biological properties. In the first place, it is responsible for the chronicity of malaria in the human organism

and, secondly, it is the cause of the persistence of malarial endemics throughout the globe.

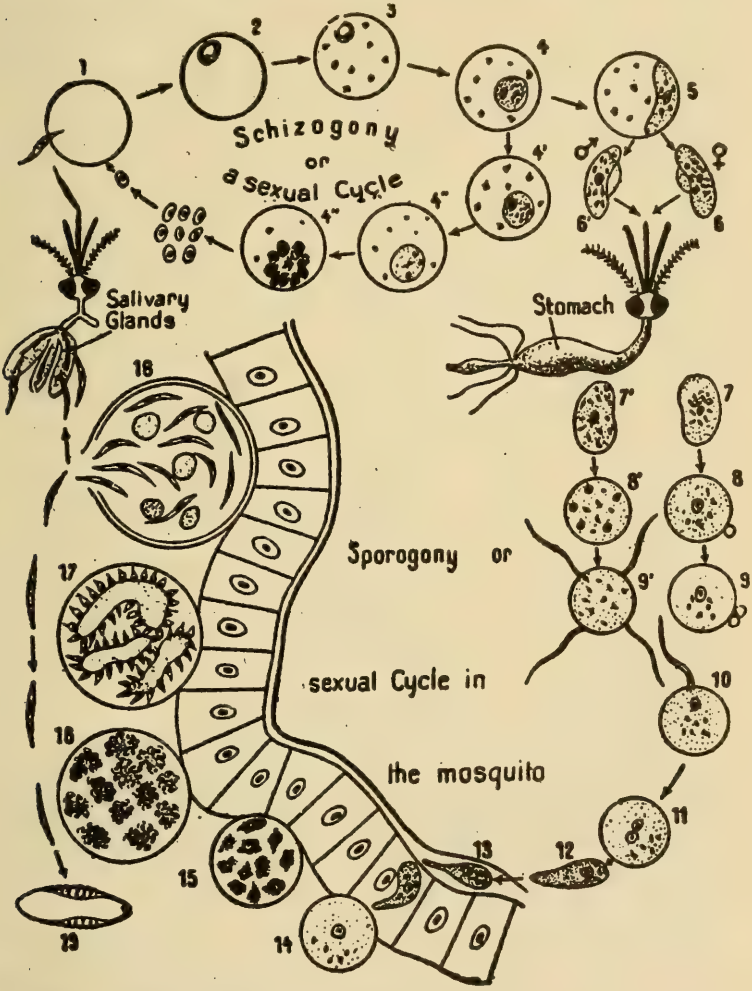

FIG. 1.—Evolution of the *Plasmodium falciparum*. *Est.*, Stomach of the *Anopheles*; *gl. sal.*, salivary glands (after Brumpt). 1, 2, 3. Schizonts. 4. Amœboid body. 4‴. Rosette body. 5, 6. Gametes. 7-11. Fecundation. 12. Zygote. 15-18. Oöcyst.

The *gamete* is extremely resistant to quinine; while the vegetative forms (schizonts, amœboid

bodies, and rosette bodies) are destroyed by the drug, the gametes may persist in the organism for months or years. Now under certain conditions when the organic resistance gives way, under the influence of fatigue or meteorological circumstances, the gametes, which had hitherto remained quiescent like parasitic cysts, begin to divide and by multiplication of their nucleus give rise to a rosette body, the rupture of which sets free the merozoites. The latter at once attack the red corpuscles, increase in size and number, and the ordinary cycle of schizogony is reproduced. This special process of segmentation of the gametes is called retrogressive schizogony or "parthenogenesis of the gametes." This is the ordinary process in relapses of malaria. It can easily be understood that as long as these special elements persist in the organism, the patient is exposed to a relapse, and it is in this sense that it may be said that the gamete, and the gamete only, keeps up the chronicity of the disease.

On the other hand, when a female Anopheles has sucked up the blood of a malarial individual, if the blood contains only the vegetative forms of the hæmatozoon (schizonts, amœboid bodies, and rosette bodies), these forms are destroyed in the organism of the mosquito. If, on the contrary, the blood contains gametes, not only do they persist in the body of the Anopheles, but they multiply in it to such an extent that in a short time the salivary glands of the mosquito are invaded by an enormous quantity of parasites, and if it bites a healthy man, it will inevit-

ably inoculate the disease. Without gametes, therefore, there would be no endemic of malaria. The development of the gametes within the Anopheles offers a very peculiar character, which

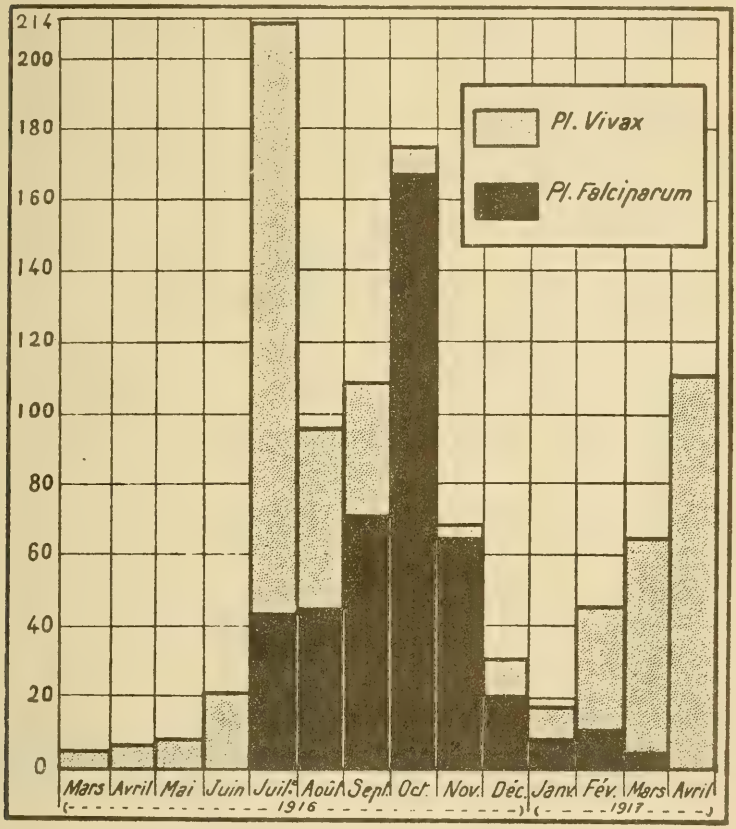

FIG. 2.—Relation of *Pl. vivax* to *Pl. falciparum* observed during the period of a year in the Army Laboratory.

we will describe in a few words. Among the gametes absorbed by the Anopheles in the blood of the malarial individual, some, viz., the *macrogametes*, behave like female elements, while others, viz., the *microgametes* (or *micro-gametocytes*), behave

like male elements. The latter protrude at their periphery a series of filaments ending in a swollen free part containing chromatin. These filaments or *flagellated* bodies become separated from the

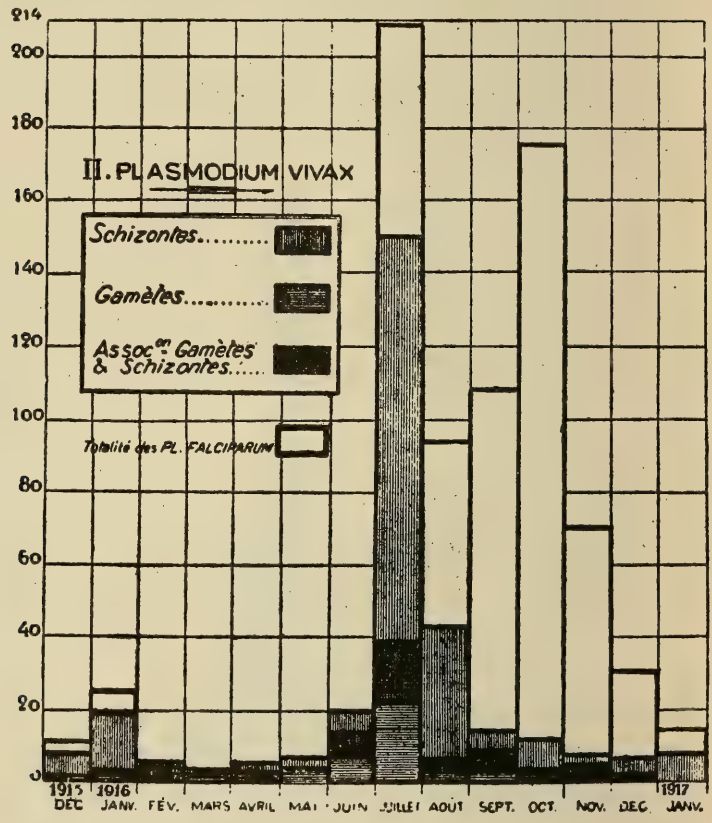

FIG. 3.—Proportion of the different forms of *Pl. vivax* (Army Laboratory).

microgametes, and make their way by movements resembling those of spermatozoa towards the macrogamete which one of them succeeds in fecundating. After fecundation, the ovum (*oökinete* or *zygote*) thus formed, becomes an

elongated, mobile element, which passes through the stomach wall of the mosquito and becomes lodged in the muscular coat of the stomach, when it increases in size and becomes surrounded by a resistant zone. It is now an *oöcyst*. This oocyst, which is derived from the fertilized gamete, becomes the seat of an active process of segmentation; its nucleolus, which is primarily single, becomes divided a very large number of times (up to 10,000). A thin band of protoplasm gathers round each of the nucleoli, and the oöcyst is thus filled with 10,000 closely-packed daughter elements, each of which is a *sporozoite*. The oöcyst on reaching maturity ruptures, the sporozoites escape, and reach the salivary glands of the mosquito, the bite of which will inoculate them into human blood.

The hæmatozoon of malaria thus presents two sharply-separated phases, one of sexual life, which takes place solely in the organism of the female Anopheles, the other of asexual life, which occurs in the human organism. In the latter reproduction of the parasite takes place in two ways (1) by schizogony, *i.e.* the formation of rosette bodies at the expense of the adult vegetative forms; (2) by parthenogenesis, or the formation of rosette bodies, at the expense of the unfertilised gametes.[1]

[1] Hitherto the process has been seen only in the female gametes or macrogametes. P. Armand-Delille, G. Paisseau, and H. Lemaire. *Note sur les constatations positives d'hématozoaires de bactériologie de l'Armée de l'Orient pendant l'année* 1916. *Bull. de la Soc. de Path. exotique.* Meeting held April 11, 1917.

The chapter on *microscopical diagnosis* contains a description of the characters whereby each of the three varieties of the hæmatozoa can be recog-

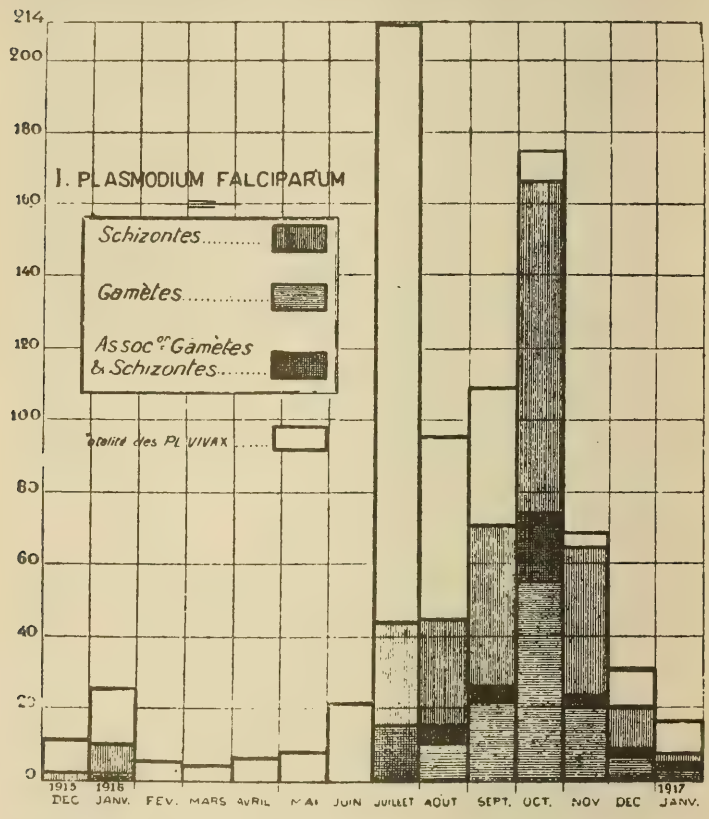

FIG. 4.—Proportion of the different forms of *Pl. falciparum* (Army Laboratory).

nized in the blood of the patient in their various stages of development.

It seems important to mention here that of these three parasites the *Plasmodium malariæ*, the agent of quartan fever, is absolutely exceptional in Macedonia, where investigations made in differ-

ent laboratories have shown it to be present in only ten cases; the *Plasmodium falciparum*, the agent of tropical fever, represents in summer (July-November) more than 85 per cent. of the cases of malaria; while the *Plasmodium vivax*, the agent of benign tertian, is rare in summer, occurring in only 15-17 per cent., and becomes very predominant from December to July.

The overwhelming majority of mosquitoes in Macedonia consist of the *Anopheles maculipennis* or *claviger*; *A. bifurcatus*, *Pyretophorus superpictus* and *Myzorhynchus pseudopictus* have been caught much less frequently. The quantity of Anopheles reaches absolutely extraordinary proportions in some regions of Macedonia, it being possible to catch hundreds of dangerous mosquitoes in a few hours.

This enormous number of Anopheles, to which Niclot, the principal medical officer, has drawn attention, possesses special interest. It is this factor which to a great extent accounts for the severity of malaria in Macedonia. In a country where there are innumerable carriers of the virus, both in the civil population and among the troops, a very large number of Anopheles are infected.

The result is that men are exposed to inoculations of the malarial virus several times a day, and this accumulation of repeated doses gives rise to a disease which is at once more severe and more resistant to quinine. Permanent and ubiquitous reservoirs of the virus, an exceptionally large quantity of the Anopheles, and the malignant nature of the parasite inoculated (*Plasmodium*

falciparum), represent the three principal factors of gravity in a malarial endemic in Macedonia. Deterioration of the inoculated subject, which is a necessary consequence of the conditions imposed on the troops as the result of war, is naturally to be added to the factors already mentioned.

Chapter II

CLINICAL STUDY

During the first months of its course in a hitherto unaffected subject, malaria is not manifested by tertian, quartan, or quotidian intermittent paroxysms, but by febrile attacks of very different types, which constitute as a whole *primary paludism*. This is clearly brought out in some textbooks on tropical medicine, especially that by Grall. We shall describe successively :—

1. A *primary paludism*, which dates from the time of infection until the appearance of the intermittent paroxysms.

2. A *secondary paludism*, characterized by frank intermittent and well-disciplined attacks, which we have chiefly observed in winter and the beginning of spring.

Primary paludism includes several phases. The first phase is called the *invasion*, which commences ten to fifteen days after inoculation, during which the patient usually presents a febrile syndrome of relatively short duration.

Then, as a rule, there occurs *a period of apyrexia*, of variable duration, during which the patient appears to have recovered. But the recovery is only apparent, as the patient for several months will present a series of febrile attacks of various

types, which constitute as a whole the *second phase*, or *phase of relapses and second attacks*.

This in turn is succeeded by secondary paludism, in which, in addition to frank intermittent attacks, we shall describe certain manifestations which only occur in the subjects of prolonged malarial intoxication.

In addition to malaria of normal evolution we shall have to describe masked and incomplete forms. It is obvious that in this short study, and even in a more didactic description, a certain number of atypical and abnormal forms liable to be met with in practice will have to be passed over.

These are the cases which can only be identified by hæmatological examination.

Chapter III

SYNDROMES OF THE FIRST INVASION OF PRIMARY PALUDISM

The phenomena characterizing the period of the first invasion of primary paludism generally assume the clinical appearance of *febrile gastric derangement.* This is the syndrome which we have observed in subjects who have recently landed ; it sometimes occurs less than three weeks after their arrival in the malarial region. It is also by far the commonest manifestation of malaria at the onset of an epidemic in the second part of June ; that is to say, in the month following the hatching of the female Anopheles. This febrile gastric derangement may assume a severe form, simulating typhoid fever, or, on the contrary, remain very slight and only be manifested by what is generally known as a feverish attack.

1. Syndrome of Febrile Gastric Derangement

During a short prodromal period of three or four days before presenting any fever, the patient suffers from vague malaise, headache, and a feeling of muscular fatigue, and the appetite is lost. He generally attributes these symptoms to the heat or to overwork. Often even he does not pay any

attention to them, and the affection appears to start suddenly with slight shivering, a rise of temperature, or a sensation of heat. The patient then complains of severe aching in all his limbs and of lumbar and epigastric pain. The headache begins in the morning and gets worse towards the

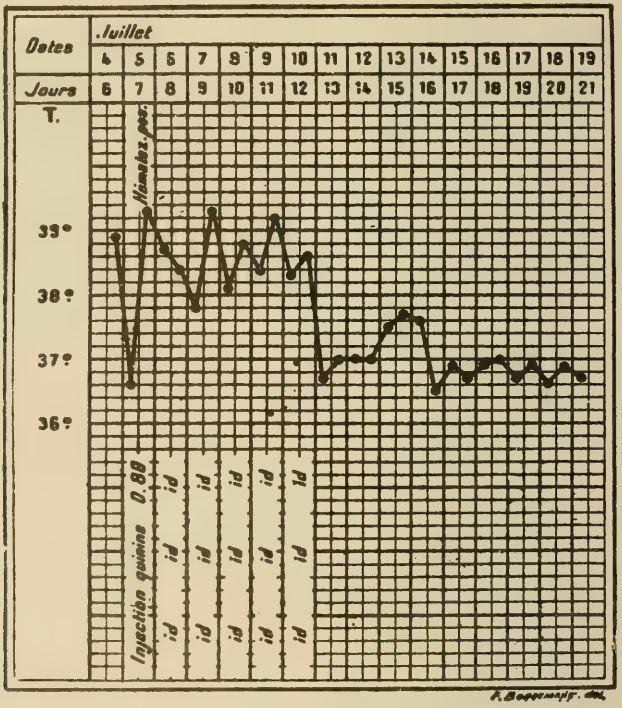

FIG. 5.—Febrile gastric derangement of the first invasion (Dr Abrami).

evening. There is absolute anorexia, the tongue is dirty and coated, vertigo and nausea are constant, and vomiting is frequent. Constipation is the rule, but sometimes a little diarrhœa of indefinite character may be noted.

Nothing definite is found on examination of the

various organs; the respiratory system is normal, the abdomen is not distended or tender, and the liver is not enlarged, but the spleen is undoubtedly increased in size. The splenomegaly, however, is slight, similar to that found in typhoid fever. By hooking the fingers under the left costal margin it is often possible to feel the lower pole of the organ, which is tender on pressure. The patient also complains of a painful dragging or stitch in the splenic region. The temperature reaches 100·4° F. on the first day, and for three, four, or even five days keeps at a level of 101·2° or 102·2°, usually with oscillations of not more than a degree. Defervescence takes place, as a rule, by lysis in two or three days at most, even without the administration of quinine, and occurs without any of the ordinary critical phenomena of the ague fit.

If the temperature be taken every hour it will be found that the daily acme takes place at the beginning of the afternoon. The pulse follows an almost parallel path with that of the fever, but increases a little more rapidly in the course of the day.

It can readily be understood that with symptoms of this kind the nature of the affection is often unrecognized, and is regarded as a mere febrile gastric derangement, a paratyphoid fever, or a typhoid fever attenuated by vaccination.

The difficulty may be further increased owing to the co-existence of an affection which is also prevalent in summer in Macedonia, viz., *Mediterranean dengue*, or three day fever.[1]

[1] *Vide* Sarrailhé, Armand-Delille, and Ch. Richet fils, *La dengue*

But the more sudden onset, intensity of the prostration, cervical and lumbar rachialgia, pains in the bones of the limbs, rapidity of course, absence of vomiting and splenomegaly, and occasionally the characteristic eruption are diagnostic features, in addition to the profound asthenia met with in convalescence, which is surprising in so short a disease.

The patient leaves hospital apparently cured, but if he has not been given sufficient quinine, he will shortly afterwards show clinical manifestations characteristic of the disease.

2. Malarial continued Fever of Typhoid character

The continued fever of the first invasion may assume a typhoid form. After a few days' malaise, the patient suddenly feels that his condition is getting worse; he is seized with shivering, intense fever, headache, generalized aching, and lumbar and epigastric pain. He is in a state of profound asthenia, exhausted and prostrate; his sleep is restless and interrupted occasionally by mild delirium. He has frequent mucous vomiting, a constant state of nausea, a thickly-coated tongue, and slight epistaxis.

méditerranéenne ou fièvre de trois jours. C. R. Acad. de Méd, Oct. 1915.

Sarrailhé, *Dengue et fièvre de trois jours. Bull. de la Soc. de Path. exotique*, Dec. 13, 1916.

Armand-Delille, *Notes sur les principaux caractères de la dengue méditerranéenne. Bull. Soc. Méd. des Hôp.*, Nov. 1916.

On examination it will be found that there is little involvement of the thoracic or abdominal organs. The abdomen is not distended or retracted, and diarrhœa is exceptional; the liver, however, reaches a little below the false ribs, and is slightly tender on pressure; the spleen undergoes some hypertrophy, which somewhat exceeds that found in typhoid fever. It is on a level with the costal margin, and is tender on palpation. The patient complains spontaneously of a stitch or a feeling of weight in the left hypochondrium. Examination of the respiratory organs is completely negative. The urine as a rule contains no albumin, and has merely the character of all febrile urine.

The pulse is quickened and very compressible, the arterial tension being definitely lowered. Its frequency is parallel with the temperature. The fever, which at the very first had risen to 103·2° or even 104·8°, keeps at this high level for a fortnight or even three weeks. On taking the temperature hourly it will be found that it begins to rise in the morning, reaches its acme at the beginning of the afternoon, and falls to the lowest level in the first part of the night.

The temperature curve regularly presents two breaks or relative defervescences, one on the fifth or sixth day, and the other on the eleventh or twelfth day. In moderate cases defervescence is sudden and final on the twelfth day; in serious cases a recrudescence takes place, and the course of the fever becomes prolonged, lasting even for a third week.

Frequently, even in the severest forms, the

continued fever gives way to a series of quotidian attacks, with large oscillations, of which the lowest

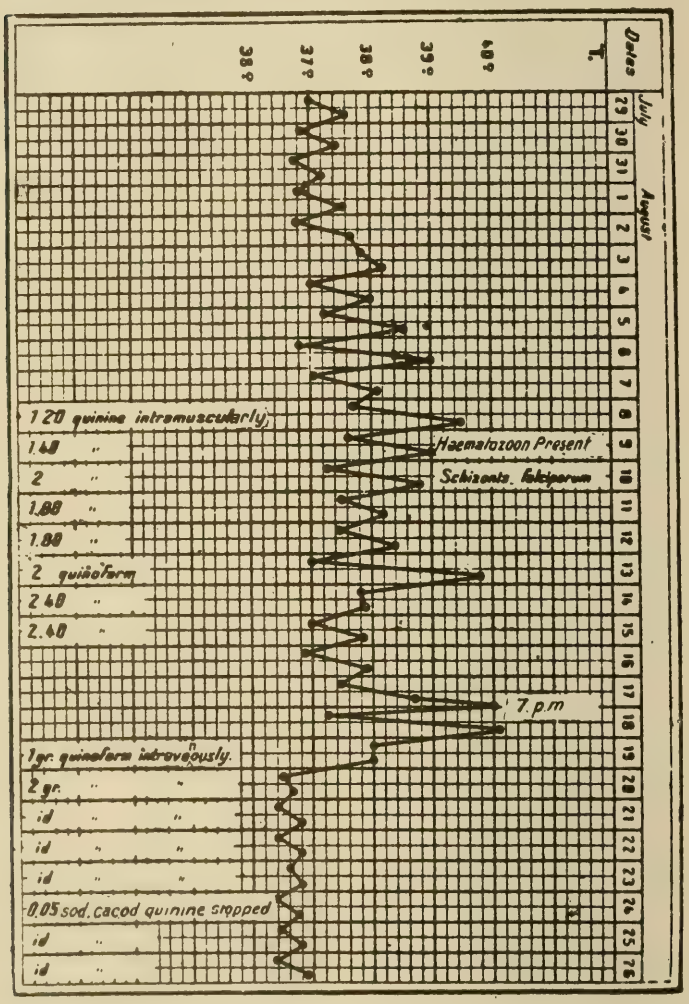

FIG. 6.—Continued malarial fever with a typhoid course (Dr Gassin).

readings are about 99·2° and the highest above 104·0° F. This daily intermittent fever lasts for

some days, and is followed by a definitive fall of temperature.

The typhoid form of the first invasion of paludism might easily be confounded with a true typhoid fever, but the rarity of abdominal symptoms, the absence of any pulmonary manifestations, and the special temperature chart are sufficient to enable the medical man who is on his guard to make a correct diagnosis, which will be confirmed by a negative typhoid blood-culture and a positive result as regards the hæmatozoon. This severe form of malarial continued fever occurs among subjects who are profoundly infected by the *Plasmodium falciparum*, their blood being rich in small annular schizonts.

3. Attenuated Form of Invasion, Febrile Malaise, and Fatigue

The symptoms of the first invasion may be much more insidious than in the two forms just described. The patient is not obliged to take to bed; for a period, which is usually fairly short, but which may vary from four to six days, he merely has a feeling of abnormal fatigue and asthenia, which he attributes to the summer heat, for the epidemic is always at its worst in the hot season.

In addition to his unusual sense of fatigue, which chiefly occurs in the early hours of the afternoon, and is accompanied by somnolence, there is considerable digestive disturbance, anorexia, and a state of nausea. The patient also suffers

from headache, which is increased by the slightest physical or intellectual effort, and often shows a daily exacerbation about midday. Lastly, in contrast with the somnolence during the day, there is insomnia at night. If the patient is a careful observer, he will notice transient febrile attacks, characterized by slight shivering, accompanied by short spells of heat and then of slight perspiration. The malaise is almost always followed by a feeling of well-being at the end of the day. The symptoms are sometimes sufficiently pronounced to necessitate temporary exemption from military duties, but often they are so slight that they escape notice.

The three syndromes which we have just described are much the most usual form of continued fever of the first invasion of malaria. Patients, however, are sometimes seen who are suffering from malaria, though their fever is of an entirely different character, viz., a fever of intermittent type accompanied by the same symptoms of gastric derangement. The fever shows great oscillations, the lowest temperatures being about 98·6°, and the highest sometimes exceeding 104° F. The attacks recur daily, constituting *quotidian intermittent fever*. The patient complains of intense headache, insomnia, pains in the limbs, and lumbo-epigastric pain. He is depressed and asthenic. His tongue is dirty; he suffers from nausea, and there is frequent vomiting of mucus. The symptoms show an exacerbation at the time of daily rise of temperature.

But, according to the opinion of numerous

writers, this quotidian intermittent fever is only apparently a manifestation of the first invasion, since on careful inquiry it will always be found that the patient had previously suffered from malaria or a febrile attack, constituting the true stage of invasion which had escaped notice.

Chapter IV

PERIOD OF RELAPSES AND SECOND ATTACKS IN PRIMARY PALUDISM

After the termination of the period of invasion, malaria enters into a silent phase in which the patient appears cured, even if he has been insufficiently treated; this period sometimes lasts from two to four weeks, rarely longer. Most of the patients return to their depôt; they may even have rejoined their unit when they again develop symptoms which may assume a considerable gravity. These symptoms are due to a relapse, or second attack of paludism. In the case of relapse there is no fresh infection, but the patient's organism has not been sterilized by the treatment; he remains a gamete carrier, and a renewed growth of the parasites takes place of varying periodicity and intensity, giving rise to fresh manifestations of the disease.

In the case of a second attack, the subject who has remained in an infected country and exposed to contagion contracts successive and frequently intense reinfections. He then presents fresh malarial manifestations, which are generally severe.

Some writers have wanted to make a distinction between a relapse and a second attack, based on clinical grounds.

As regards malaria in Macedonia, it appears to us to be impossible to establish such a distinction which, it may be said, possesses no practical importance, as the treatment should be the same in both conditions.

The symptoms which indicate relapses and second attacks do not merely present the character of general infection peculiar to the syndromes of the first invasion. The viscera are more profoundly affected, and some especially so, viz., the hæmatopoietic organs (spleen and bone marrow), the liver, alimentary canal, and suprarenal capsules. The other systems, such as the respiratory, circulatory, and nervous systems, may be involved to some extent.

The disease may assume different clinical forms as the result of the multiple localizations of the infection and their various combinations.

Sometimes the febrile manifestations predominate, giving rise to a general disease of a typhoid character. In other cases, on the contrary, the visceral symptoms become most prominent, and the patient seems to be suffering from an acute visceral affection.

Under certain conditions the general infection is so intense and violent that it causes profound changes in certain essential organs, and gives rise to a dramatic syndrome called the *pernicious attack*.

But, fortunately, malaria does not always show such pronounced symptoms, and its evolution is not always so serious. It may only be revealed by attenuated symptoms of infection, or very slight febrile attacks, when it is known as *defaced paludism*.

The fever may even escape notice, and only localized lesions indicating an organic affection are observed. This constitutes *masked paludism.*

For the sake of clearness, we shall begin by describing the principal types of the temperature curve, and we shall then study the visceral syndromes, pernicious attacks, defaced paludism and masked paludism.

1. The Temperature Curve in the Period of Relapses and Second Attacks

On reaching the period of relapses and second attacks after the silent phase, in which he might be supposed to be cured, the patient will present a series of febrile attacks of different types, and various forms of fever may be found in the same subject, either succeeding one another immediately without an interval of apyrexia, or separated by an afebrile period of varying duration.

The types of fever which we have most frequently observed are the following :—

(1) Remittent continued fever.

(2) Quotidian intermittent fever.

(3) Tertian attacks of a somewhat special character.

(4) An apparently irregular fever impossible to classify.

(1) **Remittent continued fever** is of the same type as that usually found in the period of invasion and which we have already described. In this form, in which the temperature keeps at a high level, with very slight oscillations, the daily

remissions being inconsiderable, the curve frequently presents two typical breaks towards the

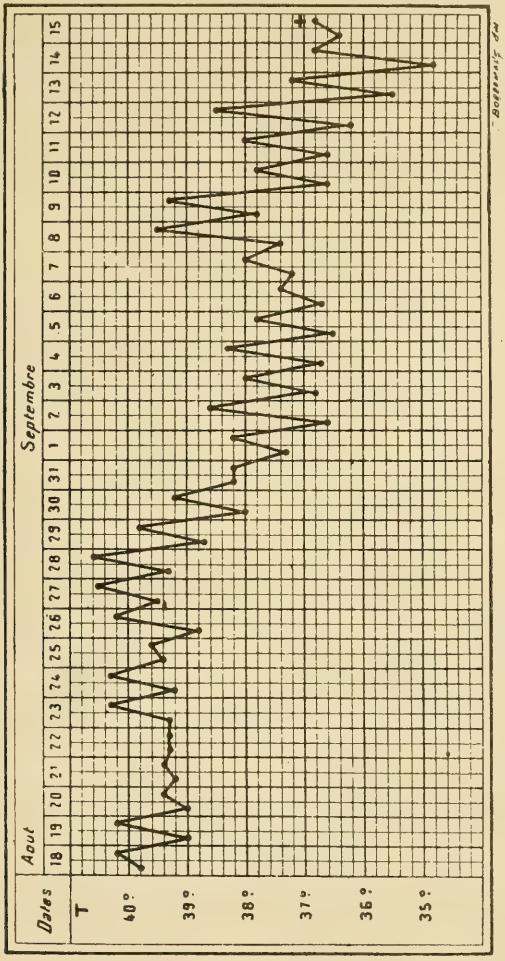

FIG. 7.—Remittent continued fever, ending in cachexia.

sixth and twelfth days, revealed by a defervescence which sometimes lasts less then twenty-four hours.

This continued fever is generally established by some ascending oscillations and the final fall of

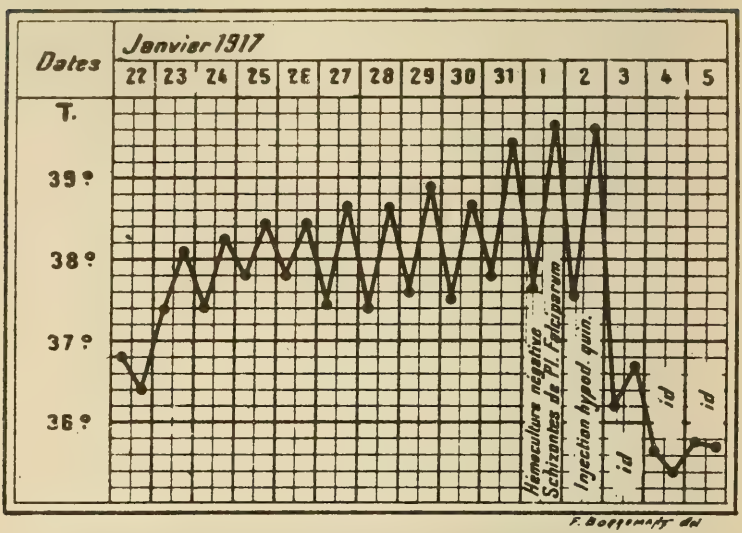

Fig. 8.—Remittent continued fever.

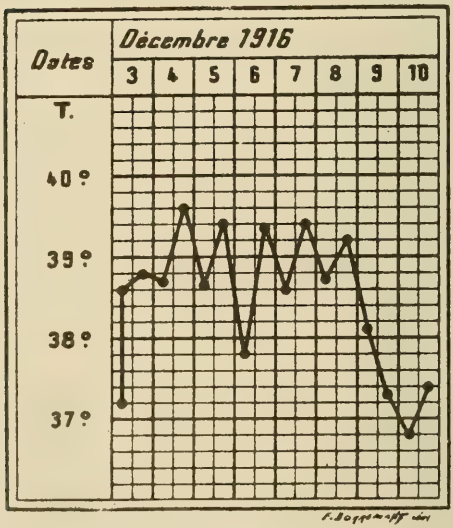

Fig. 9.—Mild remittent continued fever.

temperature, which occurs at the end of the first, second, or third week, usually takes place by lysis.

(2) **Quotidian intermittent fever** is manifested by quotidian attacks with large oscillations recurring for several consecutive days; the rise of temperature begins in the morning; at noon the maximum temperature is reached, *e.g.* 102·2°, 104°, and even 105·8° F., and keeps at this level for some hours. Defervescence begins towards the end of the evening, but is never complete, and the thermometer generally remains above 99·4° F. Quotidian intermittent fever often begins suddenly, with a rise to 104° F.

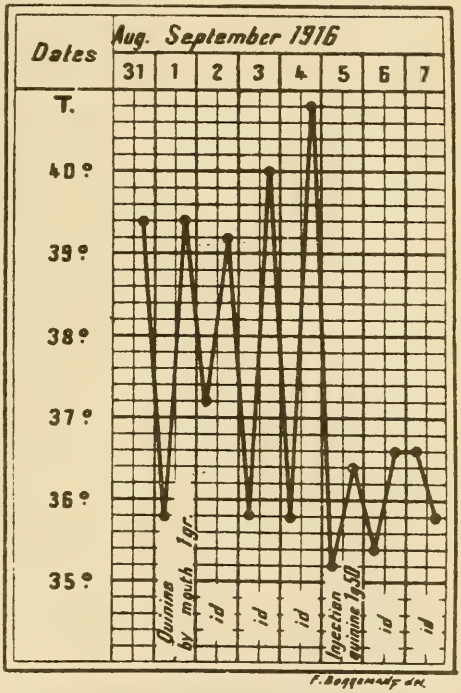

FIG. 10.—Quotidian intermittent.

(3) **Isolated attacks** occur in the midst of a phase of more or less complete apyrexia. The temperature, which in the morning was often below 98·6° reaches 104° in the first part of the afternoon, and the next morning defervescence is complete. The temperature may be even subnormal.

(4) **Attacks with a tertian grouping.**—The

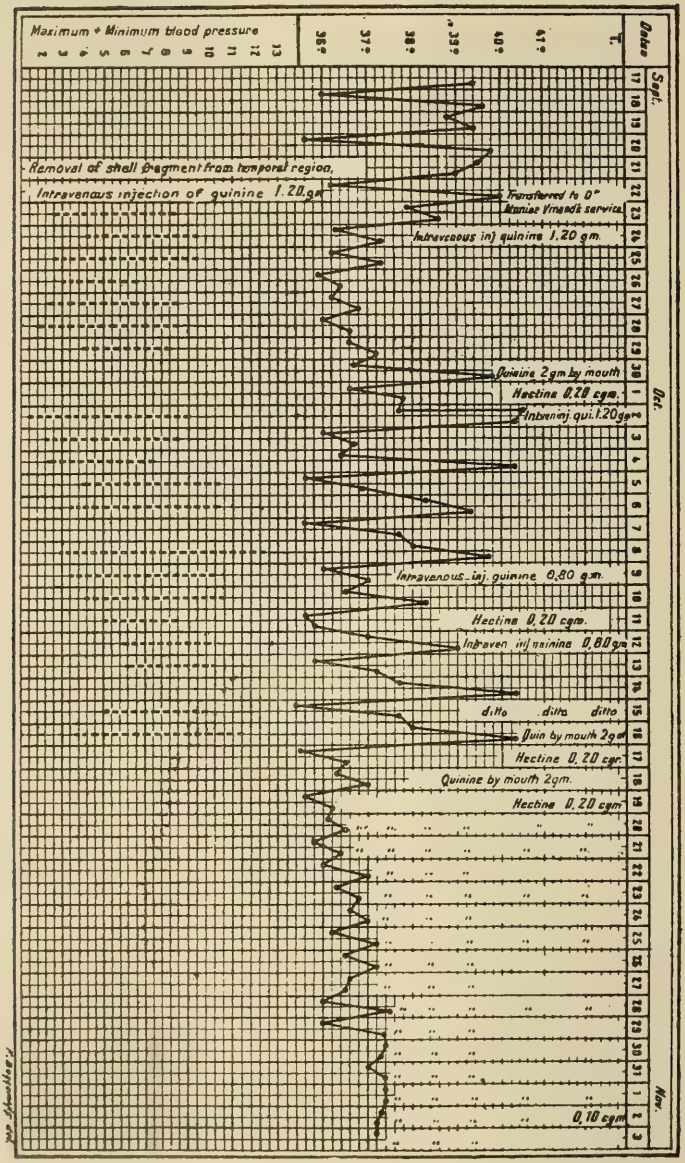

FIG. 11.—Attacks with a tertian grouping.

attacks of fever may be so grouped as to give the chart the appearance of a *fever of the tertian type.* The temperature curve, in fact, seems to be formed by a series of attacks, separated by a day of apyrexia. But on closer examination it will be seen that the apyrexia does not last thirty-six or even twenty-four hours, as in the tertian fever of the secondary period of paludism. It is much shorter, and barely twelve hours after defervescence the fever returns, the reascent is rapidly progressive, and the maximum temperature is reached thirty-six hours after the minimum and forty-eight after the previous maximum.

(5) **Irregular fever.**—Lastly, in some cases the temperature curve has an *irregular character*, which it seems impossible to analyse or classify. As a matter of fact these are often examples of quotidian attacks which are not registered on the chart because the maximum temperatures occur at a very different time from that at which the temperature is usually taken.

These different types of fever may succeed one another without an interval of apyrexia ; thus a remittent continued fever is often seen to be followed immediately by a quotidian intermittent. But as a rule the febrile attacks are separated by a phase of apyrexia of very variable duration. In most cases the apyrexial periods are of unequal length, so that no periodicity in the return of the febrile attacks can be detected ; in a large number of cases, however, a relative periodicity may be observed. This generally happens in the case of attacks occurring singly or in pairs every six or

seven days, or every twelve or fourteen days. This is known as the septan or bi-septan rhythm; the attack may even abort in the second week, and the apyretic period may then last nearly a month.

The temperature curve between the attacks does not always have the same appearance. After the attack it is not uncommon to find a slight hypothermia, the temperature being about 96·8°, and then in the days preceding the following attack it rises a degree. The apyrexial phase, therefore, seems to consist of two stages, the first being one of hypothermia, which follows defervescence from a febrile attack, and the second one, in which the temperature oscillates about 98·6° and heralds a new attack.

2. Syndromes of Visceral Localizations

These clinical syndromes, though they may vary in their localizations, have always a certain number of features in common, viz., anæmia and splenomegaly on the one hand, and asthenia and headache on the other. These symptoms constitute a minimum syndrome, which possesses considerable value in the diagnosis of the nature of a malarial phenomenon. We shall begin this section with a description of anæmia, and will then describe the gastro-bilious, suprarenal, intestinal, cachectic, pulmonary, cardio-vascular and nervous syndromes.[1]

[1] The reader must not be surprised if he does not find in these pages the redundant and confusing terminology used by most writers. We have adopted for the sake of clearness, much simpler terms which have nevertheless appeared to us to correspond to the conceptions of contemporary pathology.

Anæmic Syndromes

Anæmia.—Anæmia [1] is the almost inevitable consequence of malarial infection, and is an early symptom of it; it occurs, indeed, shortly after the end of the period of invasion at the time of the first relapse of primary paludism. When the anæmia appears, the patient rapidly assumes the special facies which indicates its nature. The face has an earthy pallor, with a dirty yellow tint most marked on the alæ nasi, ears, and labial commissures; the conjunctivæ become subicteric, and pigment patches appear on the forehead and temples resembling the chloasma of pregnancy. An earthy complexion, however, is not seen in all anæmic subjects. Some are only pale or sallow, and their skin and mucous membranes have merely lost their normal colour.

The anæmic process, once established, regularly progresses, and the clinical picture soon becomes complete. The pallor is accompanied by loss of flesh which is usually considerable, and is a special symptom differentiating malarial anæmia from a large number of other anæmic states. The patients also complain of a diminution of their physical strength, of inability to work, and pronounced asthenia; breathlessness on exertion is fairly common; digestive disturbances in the form of anorexia and attacks of diarrhœa are frequent. There is also occasionally slight epistaxis and a little transient œdema over the malleoli.

[1] *L'anémie du paludisme primaire.* G. Paisseau and H. Lemaire. *Bull. Soc. Méd. Hôp.*, June 1, 1917.

Further examination of the patient will show enlargement of the spleen, which is generally of slight degree, its lower border being on a level with the costal margin or reaching two fingers' breadths below it. The organ is tender on pressure.

The existence of extra-cardiac and anæmic murmurs in the vessels of the neck is also met with; the pulse is of decidedly low tension, exceptionally albuminuria is found, but it is always slight and transient. The anæmia continues to progress, and will increase unless quinine be administered. On the other hand, under the influence of a properly conducted course of quinine the anæmia may subside, the splenic enlargement diminish, the patient regain his weight, and his general condition improve.

Anæmia in primary paludism is not always so pronounced as we have just described it; it may even be so slight that it does not attract the practitioner's attention. In such cases it is only revealed by examination of the blood.

Anæmia in the malarial subject may assume special clinical features owing to the importance of certain symptoms accompanying it; thus we find descriptions of anæmia with hydræmia, hæmorrhagic anæmia, splenomegalic anæmia, and anæmia with icterus.

Anæmia with hydræmia.—Anæmia in malaria is often accompanied by œdema, which, as a rule, is slight and confined to the malleoli and eyelids, but it is not uncommonly seen invading the lower limbs, and even the scrotum, in which case there is considerable puffiness of the face. In exceptional

cases the œdema is accompanied by albuminuria, which is always very slight and transient. The duration of the œdema is fairly short, it diminishes in a week or a fortnight, and the hydræmia becomes an ordinary anæmia. The action of diuretics like theobromine and a chloride-free diet is nil, and does not appear in any way to accelerate the absorption of the œdema.

Hæmorrhagic anæmia.—A malarial patient with anæmia very often shows some tendency to hæmorrhages, which may, however, consist of only very slight epistaxis. But if the condition gets worse, it is not uncommon to see the hæmorrhages increase in number.[1]

Sometimes the anæmia is accompanied merely by purpura consisting of petechiæ or of ecchymoses covering the lower limbs and trunk.

In other cases various hæmorrhages are associated with this purpura, constituting a hæmorrhagic purpura, in which the patient presents obstinate epistaxis requiring plugging, hæmorrhage from the gums, hæmaturia, melæna and hæmatemesis, while hypodermic injections give rise to hæmatomata.

The anæmia is aggravated by the hæmorrhagic process, and some patients continue to bleed and die from loss of blood.

Such cases present all the clinical appearances of *progressive pernicious anœmia*, viz., a sallow skin, pallor of the mucous membranes, slight œdema of the lower limbs, multiple hæmorrhages, digestive disturbances, anorexia, vomiting, and diarrhœa.

[1] *Syndromes hémorragiques dans le paludisme.* G. Paisseau and H. Lemaire. *Bull. Soc. Méd. Hôp.*, Oct. 20, 1916.

In connection with this hæmorrhagic anæmia two points are worthy of attention. The first is the early date of its appearance, which takes place at the very onset of the period of relapses. Hæmorrhagic anæmia is most frequent in the months of July and August; later on malarial anæmia loses this hæmorrhagic character. Secondly, judicious administration of quinine causes a definite improvement in this tendency to hæmorrhages, though urgent cases may require hæmostatic treatment, such as the injection of a few c.c. of horse-serum.

Splenomegalic anæmia.—In some anæmic patients there is considerable enlargement of the spleen, which may form a veritable abdominal tumour reaching down to the umbilicus or the lumbar region, and with a longitudinal dulness of more than thirty centimetres. The enlargement of the spleen develops rapidly, and can be made to subside under the influence of quinine treatment, but the organ is slow in resuming its normal size. There is no other clinical feature characteristic of this form of malarial anæmia, and the examination of the other lymphoid organs always remains negative.

Anæmia with icterus.—We have seen that a malarial patient with anæmia often has subicterus of the conjunctivæ which is of very slight degree, and only accompanied by abnormal pigment in the urine. But it not unfrequently happens in the course of anæmia for attacks of real jaundice to occur, in which the patient's complexion becomes definitely yellow, and the urine contains normal

pigment; the stools then assume the polycholic character. The attack of jaundice, which is always of short duration, coincides with an aggravation of the anæmia, or succeeds it. We shall see later that this phenomenon is often a prelude to acute primary cachexia.

Examination of the blood.—The chief hæmatological features of the anæmia of primary paludism can be easily described.

Malarial anæmia presents every degree of severity: the number of the red cells may sometimes fall in severe cases below a million. The loss of the red cells may be very rapid, as the patient in the course of an attack may lose more than a million in a few days.

There is considerable inequality in the size of the red cells and a tendency to increase in their diameter.

Malarial anæmia does not belong to the group of chloro-anæmia, the diminution in the amount of the hæmoglobin not exceeding that of the number of the red cells.

There is generally a diminution in the number of the white cells, constituting leucopenia. Instead of 7500 to 9000 leucocytes, the numbers fall below 6000 and even 3000. Any increase in the number of the leucocytes is very transitory, or is confined to an abnormal form of cell.

The leucocytic formula shows a relative increase of the mononuclears, and therefore a diminution of the polymorphonuclears. The polymorphonuclear count, instead of ranging between 60 and 75 per cent., as it does normally, falls to 50 and

even 30 per cent., while the mononuclear count rises and even exceeds 40 per cent.

In severe cases, as soon as the number of the red cells falls to half the normal figure, elements of the bone marrow appear in the blood, viz., granular myelocytes, and even younger cells still, agranular myelocytes. Nucleated red corpuscles are exceptional or in very small numbers, even in the severest cases.

Textbooks state that the blood in malaria contains melaniferous leucocytes, *i.e.* large mononuclears stuffed full of malarial pigment. As a matter of fact these cells are very rare in the circulating blood in the anæmia of acute paludism. They are more frequent in secondary paludism. The presence of all these hæmatological characters constitutes an excellent diagnostic guide to the malarial character of an anæmia, though it does not possess the same value as the discovery of the parasite.

Gastro-Hepatic Syndromes

Gastro-bilious forms.—The febrile manifestations of the second phase of primary paludism are very frequently accompanied by gastric and bilious syndromes, which usually appear early.

The symptoms at first consist of very severe headache, anorexia, frequent bilious vomiting, and fairly profuse diarrhœa. The patient rapidly develops subicterus of the conjunctivæ and even of the skin, but his urine does not contain bile pigment. Not only does he complain of lumbar

and epigastric pain, but also of profound asthenia, with an intense feeling of fatigue. Examination of the patient furnishes more information than at the period of the first invasion. Digestive disturbance is shown by a coated though moist tongue and slight distension of the abdomen, which may be tender on palpation. The liver reaches slightly below the costal margin. The spleen is also enlarged, and to a greater extent than in typhoid fever, sometimes being one to two fingers' breadths below the false ribs, and palpation of the two organs exaggerates the spontaneous pain. The lungs are still unaffected. The heart sounds are normal, but the pulse shows an acceleration corresponding to the rise of temperature and is very compressible; the arterial tension is low, especially the minimum pressure.

This gastro-hepatic syndrome is generally accompanied by a continued fever, but the temperature curve often shows certain peculiarities. It may be immediately preceded by a quotidian intermittent of five or six days' duration; defervescence takes place by lysis, in two or three quotidian attacks, which become progressively less severe.

In grave cases prostration and adynamia dominate the scene, and the temperature, which throughout has been of the continued type, rises progressively, and the patient dies with hyperpyrexia.

In mild and moderate cases defervescence is accompanied by improvement in all the general symptoms.

Form of infective icterus.—In this form also the temperature curve consists of a succession of a continued fever and of a quotidian intermittent.

The onset is violent; the temperature rises suddenly to 104° F., the patient from the first is prostrated and plunged into a condition of profound asthenia. This state of pronounced adynamia is interrupted by mild delirium. Jaundice develops early, and rapidly becomes darker, and the urine contains bile pigment. The jaundice is accompanied by bilious vomiting and greenish polycholic diarrhœa. Hæmorrhages frequently occur, such as epistaxis, bleeding from the gums, purpura, and even hæmaturia and melæna. The tongue is first dirty and then becomes dry and shrivelled; the abdomen is distended and tender, the face drawn and pinched, the pulse weak and very compressible. The liver is two or three fingers' breadths below the false ribs, the spleen is as much enlarged if not more, and both organs are tender on palpation. Signs of congestion are found at the base of the right lung. When the general condition gets worse, the adynamia becomes pronounced, the patient grows livid, and dies from cardio-vascular collapse with an imperceptible pulse and a subnormal temperature. The clinical picture resembles, in short, that of a severe icterus, but the termination is not always fatal, as this form of icterus may end in recovery by a process resembling that of any severe icterus.

This severe form of infective icterus is, however, far from being the most frequent type. During the period of a malarial epidemic an icterus of a

mild type is much more frequently observed. This icterus appears rapidly after a short prodromal stage of gastric derangement, and is accompanied by fever, which may assume the continued or the quotidian intermittent type, or occur in the form of isolated attacks. The fever is always of short duration, and the icterus usually does not appear till the time of defervescence. The icterus has all the characters of a choluric icterus, without retention and of mild course; even when there is definite icterus the stools are not colourless, but rather pleiochromic, at least during the first few days. Examination of the organs shows slight enlargement of the liver and spleen. Splenomegaly here possesses great semeiological value, as it presents the characters of the splenic enlargement usually seen in the period of acute paludism, viz., moderate splenomegaly, in which the lower pole of the organ reaches below the costal margin and accompanied by a feeling of weight and sometimes pain in the left hypochondrium. This splenic enlargement suggests that this icterus is of a malarial character, and this suspicion will be confirmed by the negative result of an early blood-culture for typhoid bacilli and by the presence of hæmatozoa in the blood.[1]

[1] Contrary to the opinion once held it has been established nowadays that acute hepatitis and abscess of the liver are due to the amœba of dysentery, and these phenomena may naturally occur among malarial patients.

Syndrome of Acute and Sub-acute Suprarenal Insufficiency[1]

This syndrome may occur in persons whose infection is only a few weeks old. The manifestations have generally been ill-marked, and merely consist of malaise, headache, and a few febrile attacks, so that the patients keep on duty, although they become very anæmic.

Then all of a sudden a violent attack takes place, the temperature rises to 104° F. or higher, and then falls sometimes below normal to 96·8°. The attack is accompanied from the first by digestive disturbances, repeated vomiting and profuse diarrhœa. The patient complains of violent pain localized in the lumbar and epigastric regions. All these symptoms outlive the fall of the temperature and may persist till the end.

On examination of the patient the most striking thing is his statè of anæmia and emaciation; his look is profoundly altered, the features are drawn, the nose pinched, the eyes hollow, and the voice hoarse. The vomiting and diarrhœa continue, no fluid is tolerated, and there is almost absolute anorexia. The lumbar pains persist, and the patient suffers from cramps. Asthenia is the principal symptom. The patient retains his lucidity, but is motionless and in such a state of prostration that he requires an orderly to feed him, and he is incapable of sitting without support on his bed, but falls back almost lifeless; the pulse is relatively quickened

[1] G. Paisseau and H. Lemaire. *L'insuffisance surrénale dans le paludisme. Presse médicale,* Dec. 4, 1916.

(100-110), remarkably small and compressible; the arterial hypotension is not only pronounced, but reaches the lowest possible level. The phenomenon of the white line is present.

Examination of the viscera shows a normal heart and liver, but a large and tender spleen, which reaches two or three fingers' breadths below the false ribs. The reflexes are feeble but present. A fresh attack of fever may occur at this moment, exceeding 102·2° F., and in that case the symptoms get rapidly worse, the asthenia is absolute, the slightest movement becomes impossible, the temperature falls to 96·8° or even 95° F., the pulse becomes barely perceptible, and death takes place in a state of progressive algid collapse.

The total duration of these symptoms varies: the course may be very rapid, resembling an attack of cholera, so that cases of this kind have been classified under the name of *choleriform* attacks. The progress of this syndrome of suprarenal insufficiency may be more gradual, and only be fatal in about ten days' time. We have, in fact, seen transient improvement apparently due to treatment by quinine and adrenalin. The influence of adrenalin on the vomiting and diarrhœa appeared to us in some cases to be very marked; the suprarenal symptoms, however, reappeared, and the course of the disease was merely prolonged.

The syndrome of uncomplicated suprarenal insufficiency may pursue a less eventful course, and the attack may not be sufficiently severe to endanger life.

Cases of this kind may be classified in two distinct categories. In the first the syndrome of suprarenal insufficiency remains exclusively glandular, while in the second it is complicated by the pigmentation characteristic of Addison's disease.

The first group consists of recently infected patients, whose symptoms during the first invasion did not show any features of abnormal gravity. After presenting these symptoms they remain anæmic and show slight digestive disturbances, such as nausea, occasional vomiting, and anorexia, but their chief symptom is profound asthenia. They are confined to bed in a condition of prolonged immobility, and are incapable of the slightest muscular effort. Their pulse is easily compressible; with Pachon's oscillometer we found a minimum tension of 2° and a maximum of 9°. On questioning them it is found that they frequently suffer from pains in the lumbar regions. Their general condition did not appear grave; when treated methodically their symptoms appeared to improve, and the patients could be evacuated.

This syndrome of gradual suprarenal insufficiency may be completed by the appearance of pigmentation. The pigment spots are situated in the usual situation, viz., the temples, scrotum, and buccal mucous membrane. The syndrome of Addison's disease is then complete.

Intestinal and Peritoneal Syndromes

Diarrhœic and dysenteriform symptoms.—Intestinal disturbances are fairly frequent in malaria.

They consist of diarrhœa and dysentery. The character of the diarrhœa varies in gravity.[1]

As a rule there is merely an attack of bilious diarrhœa associated with an isolated paroxysm or a short series of quotidian attacks. The intestinal catarrh begins and ends with the fever. The patient has about ten stools in the twenty-four hours. The evacuations are abundant, liquid, bilious, mucous, and bloody. Each stool is accompanied by more or less diffuse abdominal pain, but often most pronounced along the transverse and descending colon.

The diarrhœic syndrome presents several relapses. A malarial patient who has previously had symptoms of entero-colitis during a febrile attack, is subject to fresh outbreaks on each subsequent febrile attack. It may often happen that the only manifestation of some malarial attacks is a diarrhœa, which serves as the equivalent of a malarial attack, febrile or otherwise. These outbreaks of malarial entero-colitis are improved or cured by quinine. But the intestinal disturbances in malaria may assume a more severe form, the diarrhœa being complicated by a dysenteriform syndrome, especially in patients suffering from more or less severe continued fever. The diarrhœic syndrome which at first is most in evidence is shown by very frequent bilious discharges and more or less abundant and repeated intestinal hæmorrhages, but tenesmus and rectal gripping are soon added to the phenomena of entero-colitis,

[1] P. Abrami and C. Foix, *L'entérite du paludéen. Réunion des Soc. Méd de l'A. O.*, Nov. 7, 1916.

the stools become more and more numerous, and take on the " frog-spawn " appearance of dysentery. The dysenteriform syndrome has now taken the place of the initial bilious diarrhœa. The patient's general condition changes, his face becomes pinched, his voice becomes weak, and he dies in a sort of typhoid state.

This dysenteriform syndrome sometimes occurs so early that the patient appears to be suffering from actual dysentery from the very first. The intestinal manifestations of malaria should always attract the doctor's attention, as their tendency to recur and to become chronic predisposes to a serious complication, viz., acute primary cachexia, of which we shall speak ater.

The diagnosis of the nature of these dysenteriform states is often difficult owing to the frequent co-existence of amœbic or bacillary dysentery during the season of a malarial epidemic. Apart from laboratory information, the character of the fever accompanying these symptoms will enable the course to be established in the great majority of cases.

Peritoneal Syndrome

The patients are sometimes brought to hospital with the diagnosis of appendicitis, as in the course of a febrile attack they are seized with vomiting and diffuse and violent lumbo-abdominal pain. The tenderness of the abdomen is so exquisite as to suggest a peritoneal reaction, especially as the pulse is often very compressible, but the presence

of diarrhœa, the absence of precise localization of the pain, and the course of the symptoms which rapidly subside, negative the idea of appendicitis, which at first seems absolutely certain.

Syndrome of Acute Cachexia

During the period of relapses in primary paludism we have sometimes observed a syndrome of considerable gravity, viz., a sort of cachexia of rapid course, ending fatally within a few weeks.[1]

This syndrome develops in patients who have generally had only very slight symptoms during the first invasion. The symptoms merely consist of a sense of fatigue or such mild digestive disturbances and transient febrile attacks that the patient does not want to be admitted to hospital, and owing to the mild character of the symptoms the period of invasion escapes notice, and the subject does not undergo any special treatment.

During the following weeks the patient appears to become decidedly anæmic. The anæmia may occur without fever or on the occasion of a febrile attack, which seems to be the first manifestation of the malarial infection, whereas it is already a phenomenon of the period of relapses. The syndrome of anæmia pursues a progressive course, and is almost always accompanied by fever, which assumes one of the types which we have previously described, viz., the continued form, the quotidian intermittent, or the tertian variety. All these

[1] G. Paisseau and H. Lemaire, *La cachexie aiguë du paludisme primaire. Bull. Soc. Méd. Hôp. de Paris,* Dec. 8, 1916.

types of fever may be met with in the same subject succeeding one another without an interval of apyrexia.

Anæmia is not the only symptom which plays a part in this cachectic syndrome. Profound asthenia and digestive disturbances, such as vomiting and diarrhœa, rapidly supervene. At first these symptoms may be only intermittent, not developing until the outbreak of fever, and ceasing in the phase of apyrexia. During the patient's attacks of fever the vomiting and diarrhœa assume an almost uncontrollable character, the asthenia is profound, the lumbar pain is very severe, and the arterial tension is particularly low. It may often happen that these symptoms, especially the digestive disturbances, last longer than the fever, and outlive the attack which seems to have caused them. A sudden aggravation soon becomes obvious ; on the occasion of a particularly violent febrile attack the vomiting becomes more intense, the stools more frequent, and the asthenia more profound than they have ever been before. The anæmia also increases, and an icterus often appears, which, as a rule, is transient and mild and not accompanied by normal bile-pigment in the urine. Breaking up of the organism now speedily takes place, and emaciation proceeds very rapidly. The appearance of patients in a state of cachexia is particularly striking, the subject is profoundly anæmic and has an earthy, dirty yellow complexion, his mucous membranes have lost their colour, and the conjunctivæ are often subicteric. Emaciation is extreme, especially in the face, where the skin

appears stuck to the bone, and the combination of all these changes gives the face a remarkable appearance of precocious senility. Asthenia is an important symptom; the patient is confined to bed, as every movement is a source of fatigue, the arterial hypotension is pronounced, the minimum tension falling to a very low level. Bed-sores develop. Digestive disturbances still dominate the scene: vomiting occurs whenever the patient attempts to take food, the diarrhœa is often profuse, and both the vomiting and diarrhœa occasionally assume a hæmorrhagic character.

Further examination of the patient shows slight enlargement of the spleen, which reaches or just passes below the level of the false ribs; the liver is also somewhat enlarged and tender on pressure, but the other viscera show nothing abnormal.

This syndrome of acute cachexia which we have only observed in malaria due to the *Plasmodium falciparum*, has almost always a fatal issue. But we have seen a case which threatened to be fatal arrested by intensive treatment with quinine associated with adrenalin. In our opinion this successful result can only be obtained when the digestive disturbances and emaciation are not too pronounced.

Pulmonary Syndromes

During the period of relapses and second attacks the malarial patient may present pulmonary manifestations, the clinical features of which are characteristic enough to justify their being attributed to malaria.

Four varieties of these syndromes may be distinguished.

The first, which is by far the most frequent, is a *mild form*; it is characterized either by signs of disturbance of function occurring in the course of an attack and consisting in a spasmodic and paroxysmal cough with some respiratory distress, or by signs of slight bronchitis; the former disappear with the attack, and the latter persist.

An equally frequent form is *bronchitis with pleuro-pulmonary congestion.* The patient is re-admitted to hospital for pain in the chest, cough, dyspnœa, and fever. On examination all the signs of pleuro-pulmonary congestion are found accompanied by bronchitic râles. For two or three days one does not think of malaria, as there is nothing to indicate it. But one soon becomes struck by the changing character of the stethoscopic signs, which increase, subside, or shift their position in less than twenty-four hours; the patient's symptoms and general condition present the same remissions and exacerbations. These manifestations of pleuro-pulmonary congestion are accompanied by one of the types of fever usually observed at this period of the disease. They are mild in character, and almost always end in complete recovery, often in less than a week. In some cases, however, the stethoscopic signs persist for some days after defervescence, signs of dry pleurisy or even of a slight pleural effusion being found.

The two other forms which we have observed are much rarer.

One of them suggests a *pneumonia* of the apex.

The typical signs are present, such as dulness, bronchial breathing and crepitant râles, but the sputum generally remains viscid and only exceptionally assumes the characters of that of a frank pneumonia. This form of pneumonia often relapses *in situ* or in another part of the lung. Its course runs parallel with that of the fever, and is definitely influenced by quinine.

Lastly, we may find in malaria the typical picture of *pulmonary apoplexy* which often has a rapidly fatal termination; but this complication is, fortunately, very exceptional.

Cardio-Vascular Syndromes

The circulatory system does not always escape in the course of primary paludism. We have chiefly observed disturbance of the peripheral circulation and in the extremities of the limbs. These circulatory disorders present all degrees of severity, ranging from Raynaud's disease to *symmetrical* gangrene of a considerable segment of a limb. Raynaud's disease in its attenuated form may take on the cyclical course of a malarial paroxysm with exacerbations and remissions parallel with those of the fever. In the severest cases it may be permanent and be associated with small areas of sloughing. Patients suffering from this complication, who have contracted a severe infection, find that their lesions are improved and cured by quinine.

Symmetrical gangrene of the limbs which usually involves the feet and the lower third of the legs,

has a more rapid and acute course. We have seen it occur in febrile attacks of malaria, and frequently in the course of pernicious attacks.[1] The patient generally dies of malaria, but we have seen a case which recovered through the combined action of quinine and adrenalin in intravenous injections. For the sake of completeness we may mention that some cases of erythromelalgia have been attributed to malaria. The peripheral circulation is not the only one affected. The visceral arteries present lesions of endarteritis like those of the peripheral arteries, which accounts for the unexpected occurrence of visceral syndromes in acute paludism. Among the latter, especially affecting the circulatory system, we should like to draw attention to the occasionally fatal attacks of angina pectoris with changes in the coronary arteries.

Urinary Syndromes

Urinary syndromes are exceptional in primary paludism. The only examples of this kind which we have seen have been a few cases of albuminuria occurring at the time of the febrile paroxysms. The albuminuria was always slight and transient. As a rule the patient was suffering from decided anæmia, and had been admitted to hospital for this complication of malaria. In the patient's past history we have more than once met with

[1] Alamartine, *Soc. des Sciences Méd. A. O.*, 1916. Paisseau and Lemaire, *Deux cas de gangrène palustre. Bull. Soc. Méd. Hôp.*, Feb. 9, 1917. Laurent Moreau, *Presse médicale*, March 22, 1917.

an illness like severe scarlet fever which might account for a previous renal affection.

In three cases, however, we observed a real acute nephritis in every way resembling that of secondary syphilis including massive albuminuria to the amount of 15-30 grammes in the twenty-four hours, and a considerable degree of œdema. In two cases quinine caused the phenomena to subside rapidly. In the third case, on the contrary, it aggravated them.

Early bilious hæmoglobinuric fever.—At the height of the malarial epidemic in August and September we saw some cases of hæmoglobinuric fever in patients who were in the period of relapses of primary paludism, but these cases were exceptional. Most of the cases of bilious hæmoglobinuric fever occurred in the cold season at a later stage of primary paludism, or more frequently, in the course of secondary paludism. We will, therefore, reserve the description of this complication for the last period of the disease, where will also be found an account of the clinical features of bilious hæmoglobinuric fever of the period of relapses, the prognosis of which is always very gloomy.

Nervous Manifestations

The changes in the nervous system have been specially studied in the hospitals at Salonica by our friend and colleague Dr Monier-Vinard, to whom we are indebted for the following information.

Nervous symptoms, apart from those corresponding to the meningeal reaction observed in the forms which are severe from the onset,[1] as a rule do not occur until several months after infection, and often only in the course of secondary paludism; and it is, therefore, in autumn and winter that they are most frequently observed. They may be divided into neuralgia, neuro-muscular disorders, and polyneuritis. Occasionally focal lesions of the nerve centres may be observed.

Neuralgia.—This most frequently affects the ophthalmic branch of the trigeminal nerve, and is often accompanied by trophic lesions of the eye and its appendages, as we shall see later, as well as by palpebral and labial herpes zoster. Sciatica is also a favourite localization.

All the varieties of malarial neuralgia have features in common; they are generally unilateral, present periodic paroxysms, especially in the night or morning, and are unaffected by most analgesic remedies, while they are, on the contrary, remarkably influenced by quinine.

Neuro-muscular disturbances. — These are chiefly seen in patients who have been subject to fatigue and belong to the group of cases for which Babinski has suggested the name of *physiopathic disturbances*. The symptoms are chiefly *motor*, sometimes both sensory and motor, being characterized by muscular cramps, usually situated in the calf but occasionally affecting a large number

[1] Monier-Vinard, Paisseau, and Lemaire, *Cytologie du liquide céphalo-Rachidien au cours de l'accès palustre. Bull. Soc. Méd. Hóp.*, Oct. 20, 1916.

of muscles. The cramps often co-exist with febrile attacks.

Muscular hypertonus may also be observed, being revealed objectively and subjectively by muscular rigidity frequently existing with muscular asthenia.

Exaggeration of the tendon reflexes is the rule, idio-muscular excitability on percussion is increased in the affected muscles, and electrical examination shows, according to the case, the myasthenic reaction, the myotonic reaction, and more rarely the galvanotonic reaction.

The motor phenomena are sometimes associated with anæsthesia to pricking and even to burning, with a segmental or radicular topography. Cyanosis with slight swelling of the extremities is also very frequently met with, and the patients then complain of a sensation of cold and numbness. Pollakiuria is often present, being due to changes in the excitability of the cord.

The natural course of these symptoms is to end in recovery, though this may require weeks, and often even months.

Polyneuritis.—This seems to be rarer than some authors have stated. Other toxic and infective processes which may be associated with the malarial infection must be taken into account. During the cachectic stage of the disease, however, diffuse polyneuritis may be observed, manifested in the limbs by diminution of the reflexes, wandering pains and even muscular atrophy.

Focal lesions.—These are due to the same process as the meningeal hæmorrhages and are

almost always the result of a congestive attack. They are relatively rare. They may present the characters of a simple hemiparesis or a paralysis of the Weber or Millard-Gubler type. Right hemiplegia with motor aphasia has sometimes been observed.

Mental disorders.—These have been specially studied in the army of the East by our friend Dr Vinchon, who has supplied us with the following information.

Malaria, like all other infections, may be associated with mental disorders, the origin of which may be explained by the patient's antecedents, whether hereditary (degeneration) or acquired (alcoholism). These disorders, which occur in all stages of the disease, appear in several forms, such as delirious or convulsive attacks and asthenia. Moreover, the course of pre-existing psychoses is accelerated or aggravated.

The attacks of delirium are of varying duration and consist of two types: 1. *Mental confusion* with oneiric delirium. 2. *Melancholia* with anxiety without confusion.

The first form is the more serious of the two; physical signs, such as a tendency to cardiac collapse and dyspnœa, are a bad prognostic. In the second form, which is milder, the delirium may or may not disappear with the fall of the temperature; if it persists, as well as the physical disturbances, a relapse is to be feared, in which death often occurs with hyperpyrexia or with a subnormal temperature, after a fresh attack.

Convulsions, which are chiefly due to congenital

predisposition are attacks resembling those of hysteria, and sometimes begin with severe pain in the splenic region. Malarial asthenia, whether it occurs early or late, is aggravated and prolonged by anæmia, but in some cases it may persist after the latter has disappeared. Malaria causes a return of attacks of periodic psychosis, a more rapid evolution of dementia, and an aggravation of hypochondriacal or persecutional delirium, based on hallucinations or delirious interpretations. The treatment is that of malaria associated with that suitable for mental disorders. Heliotherapy, as well as hydrotherapy, yields excellent results. Lastly, in the course of attacks of delirium or asthenia, malaria gives rise to medico-legal complications, especially fugues and attempted suicide.

Ocular Complications.

These have been studied in a very large number of cases by our colleague and friend, Dr Chavernac, who is in charge of the ophthalmological department, and we are indebted to him for the following information. The complications may affect the nerves of the eye and its vascular system.

Symptoms of affection of the sensory nerves.—*Keratitis* is frequently observed, being closely associated with neuralgia of the trigeminal, and generally occurs from two to three days after the paroxysm which was the cause of it. It is usually accompanied by palpebral herpes and is almost always complicated by *iritis* with slight hypotonus of the eyeball.

It is superficial and slight in the case of infection by the plasmodium vivax, but obstinate and difficult to cure in the case of plasmodium falciparum infection. It may assume any of the following types : phlyctenular, vesicular, dendritic, annular, disciform, nodular, striated or ulcerative marantic.

To effect a cure it is necessary to adopt an intensive quinine treatment as well as local treatment with atropine. *Secretory disorders* may be observed in the form of lacrymation lasting several hours during the neuralgic paroxysm.

Symptoms of affection of the motor nerve.— These consist either in affection of the extrinsic muscles, such as paresis or permanent paralysis, involving especially the superior rectus, the external rectus, or the muscles of convergence, or in affection of the intrinsic muscles, causing paresis or cramps of accommodation.

Symptoms of affection of the optic nerve.— These consist of subjective phenomena, such as transient or permanent amblyopia, coloured vision (erythropsia, cyanopsia, xanthopsia), hemeralopia and hemianopsia. Hemianopsia was found to be excessively frequent, several hundreds of cases having been observed, almost exclusively in the hot season.

Quinine amaurosis, on the contrary, was exceptional, in spite of the considerable number of cases under treatment. Only one case was seen by Dr Chavernac, so that the apprehension of this complication should never be a contra-indication to the use of large doses of quinine.

Changes in the vascular system.—*Conjunctival hæmorrhages* are frequent, but have no effect on vision.

Iritis is a frequent complication of keratitis, but rarely exists as an isolated phenomenon. It is influenced by the febrile attacks, which may provoke, aggravate, or prolong it, but it subsides without leaving any trace.

Uveitis of protracted course was observed in two cases.

Chorio-retinitis is very frequent in individuals who have been infected several months previously, and appears in the form of peri-papillary deposits of pigment, the abundance of which may cause a diminution of vision. Quinine has no action upon them.

Congestion of the retina is a common occurrence in the course of an attack, the veins are swollen and the macula is dark red.

Exudations appear in the form of slight greyish films masking in places the outline of the vessels; they may even run together and form an agglomeration with circular outline.

Retinal hæmorrhages are macular or peri-papillary, and pre-retinal, intra-retinal, or retro-retinal. They usually become absorbed fairly quickly, but they may give rise to atrophy of the retina. They are easily seen with the ophthalmoscope, and are always situated in the area supplied by the short posterior ciliary arteries.

Laryngeal and aural complications.—The laryngeal complications of malaria which have been studied by our friend Dr de la Mothe are

almost exclusively of a motor character. We have, in fact, never come across a case of laryngeal inflammation which could be undoubtedly attributed to malaria.

Aphonia may develop more or less suddenly, usually after severe attacks and almost always in association with marked asthenia. The voice is faint, whispering and toneless, being interrupted owing to the waste of the air column, the glottis closing incompletely.

This aphonia may be due to two causes. 1. More or less pronounced paresis of the constrictors of the glottis and tensors of the vocal cords.

2. A true recurrent paralysis of one vocal cord, which is less frequently met with and may or may not end in recovery. The prognosis is favourable. As regards treatment, one should wait until the state of asthenia has disappeared. A few courses of faradization and re-education will then be enough to restore the patient's voice.

Two other exceptional conditions have been observed :

1. A case of paralysis of the dilators of the larynx, the right vocal cord being immobilized in the median position. This phenomenon being unilateral was not accompanied by any disturbance of function. It is reasonable to suppose that in some cases this paralysis may be double, the glottis being entirely closed, in which case intense respiratory distress will develop and necessitate tracheotomy.

2. Several cases of motor inco-ordination,

difficult to interpret, in which the laryngeal disorders are associated with disturbance of speech resulting from the affection of other centres.

Auditory disturbances.—In our opinion there is not such a thing as quinine deafness. All the patients admitted to hospital with this diagnosis whom we have seen up till now were suffering from old lesions of the middle ear. Quinine causes a temporary congestion and gives rise to tinnitus, but these auditory disturbances are transient and disappear rapidly without leaving any trace.

We have had no opportunity of seeing a case of deafness from affection of the labyrinth or the cochlear nerve due to malarial infection. On the other hand, we have observed two cases of disturbance of equilibrium with loss of excitability of the vestibular nerve. Both cases improved.

3. Pernicious Attacks

Throughout the period of primary paludism, often even within the first weeks following the invasion, the malarial patient may present symptoms of such special gravity and with such a violent and dramatic course that they have been entitled *pernicious attacks.*

This *pernicious character,* to which some writers have tried to attach a mysterious significance, is simply due to the association of two factors: invasion by a large number of parasites and diminution of the resistance of the organism. In all cases under our observation examination of the blood during life and before quinine treatment,

frequently showed an enormous proportion of the red corpuscles affected by the parasite ; on autopsy the visceral capillaries were crowded with hæmatozoa always belonging to the variety of *Plasmodium falciparum*. Furthermore, persons suffering from pernicious attacks are generally men who have been subjected to overwork and fatigue.

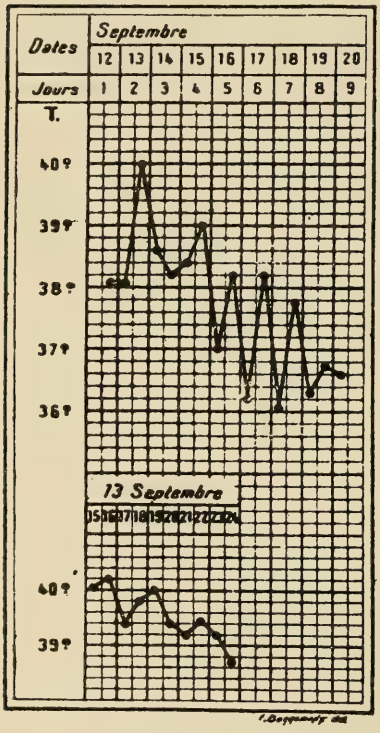

FIG. 12.—Pernicious attack, of the apoplectic type.

This intense parasitic invasion, associated with these causes of breaking down of the organic resistance, offers an explanation of the profound lesions always observed in some viscera such as the nerve centres and the suprarenal capsules.

The pernicious attack generally occurs in an individual who appears to be in perfect health and is suddenly taken ill while engaged in his ordinary duties. But it may also develop in a patient already under treatment for some malarial manifestation. A rapid and unexpected aggravation ensues, which may cause death in less than forty-eight hours.

It is usual to describe a large number of types

of pernicious attacks, *e.g.*, the cerebral, algid, delirious, bilious, diaphoretic, choleriform, gastralgic, cardialgic, dyspnœic, etc.

We will describe only two sorts of pernicious attacks, viz., the *cerebral attack* and the *algid attack*, for the cases which we have observed, and which might be regarded as other forms of pernicious attacks, did not seem to us to present a sufficiently violent and rapid course to justify their classification among these forms of malaria.

Cerebral forms.—The cerebral attack presents two clinical types: *the apoplectic attack* and *the convulsive attack.*

Apoplectic attack, insolation type.—The patient is suddenly seized in the middle of his work with symptoms resembling those of heat stroke. He has merely been complaining of fatigue, headache, and insomnia for a few days, when all of a sudden he becomes giddy and falls down in the road in a state of apoplexy. His face is bloated and his respiration sighing. He presents conjugate deviation of the eyes and complete muscular relaxation. The last symptom, however, is often succeeded by slight hypertonus, especially in the upper limb, as indicated by flexion contracture of the forearm: the deviation of the head and eyes is not always conjugate, but is often opposed. These two symptoms indicate a cortical localization with a meningeal reaction, which is confirmed by the existence of a cerebro-spinal lymphocytosis.

The patient's temperature rises at once 103·2° or 104°, or even 105·8° F. Death may occur in a

few hours. In other cases some improvement may take place in twelve to eighteen hours' time. The patient gradually wakes up out of his torpor, asks some questions and calls for a drink. If examination of the blood has been made and any kind of injection of quinine has been given, especially an intravenous one, improvement takes place very rapidly, the temperature falls progressively in two or three days, or on the other hand the patient remains febrile and presents a sub-continuous fever, which is usually very little affected by quinine. This apoplectic attack is sometimes accompanied by signs of focal lesions, *e.g.*, hemiplegia or aphasia.

Hemiplegic variety.—In some cases a unilateral predominance of the symptoms of paresis may be found at the time of the loss of consciousness, constituting an actual hemiplegia or hemiparesis. The course is the same as in the previous case. The paretic phenomena disappear entirely under the influence of quinine, and the patient recovers consciousness simultaneously.

Aphasic variety.—Before the comatose period or when it is passing away, some patients may show, either with or without a right-sided paresis, symptoms of motor aphasia, which may last some hours, but also yield to treatment.

Convulsive meningeal form.—The pernicious attack starts with convulsive phenomena of the epileptiform type, which may simulate a true attack of epilepsy; there is also contracture of the limbs, nuchal rigidity, and sometimes conjugate or dissociated deviation of the head and

eyes, accompanied by persistent coma with a rise of temperature to 104° or 105·8° F. Examination of the blood and discovery of the causal agent lead to the adoption of quinine treatment. We may add that in these cases the cerebro-spinal fluid shows considerable lymphocytosis, definite albumin, and slight hypertension.

In some cases transient coma is met with, accompanied by icterus, vomiting, and bilious diarrhœa. These phenomena correspond to the *bilious attack* described in textbooks.

Algid form.[1] — In this well-known form of pernicious attack the patient's appearance is characteristic ; the initial symptoms are often the same as in an ordinary attack, but the fever is particularly high. It is accompanied by nervous disorders, which are sometimes intense, delirium, and almost uncontrollable vomiting.

But the picture suddenly changes completely, the temperature drops, falling to 96·8° and lower, and the various symptoms of algid collapse set in.

The patient then presents a characteristic appearance. He remains quite still, in a condition of profound asthenia, the face is drawn, the eyes sunken, fixed and expressionless ; the nose pinched and the voice hoarse. The face is often discoloured by violet patches, the extremities of the hands and feet are cyanosed and cold as ice, the skin covered with clammy sweat, and the respiration is shallow. The pulse is only slightly accelerated,

[1] Paisseau and Lemaire, *Accès pernicieux palustres et surrénalite aiguë. Bull. Acad. Méd.*, Oct. 17, 1916, and *Bull. Soc. Méd. Hôp.*, Oct. 13, 1916.

and is small and compressible, and the arterial pressure is very low; we have noted the phenomenon of the white line. The heart sounds keep their normal rhythm, but are simply weakened.

This syndrome of algidity and hypotension is very often associated with a series of secondary symptoms chiefly affecting the alimentary canal. There is repeated vomiting, accompanied by profuse diarrhœa and lumbar, abdominal and epigastric pain, and the patient often complains of painful cramps. The picture of a choleriform attack is thus complete. Death may occur suddenly, consciousness being retained till the end. When the attack ends in recovery, which is exceptional, the arterial tension rises as well as the temperature, the extremities become warm again, and abundant perspiration develops, marking the end of the attack. The algid attack is of the utmost gravity, but there is, nevertheless, some hope of saving the patient by the combined action of quinine and adrenalin in intravenous injections.

4. Defaced Paludism and Masked Paludism

Defaced paludism.—Defaced paludism may be regarded as an attenuated form of malarial infection. It is found in persons who have been only very slightly exposed to infection, or in those living in easy circumstances and possessing a sort of natural immunity. It is a kind of almost apyretic paludism, in which the visceral localizations are few and slight. The initial manifesta-

tions consist of an ill-marked febrile malaise. They may be so trivial that they pass unnoticed by patients who do not pay much attention to their ailments.

Subsequently, instead of the febrile attacks of the period of relapses and second attacks, the patients have incomplete attacks only. Fever, though often denied, is not completely absent, but is slight and curtailed ; it has, as a rule, completely disappeared when the other symptoms attract the patient's attention. These symptoms are mostly of a subjective character, such as neuralgia, headache, lassitude, and asthenia, which are succeeded by a sense of well-being. Close examination suggests a certain degree of anæmia, which is confirmed by hæmatological examination, and can often be found in this way even in persons of florid appearance. This anæmia has the hæmatological appearances of the malarial anæmia which we described above. It consequently possesses a real semeiological value. Its presence, if it does not actually warrant a certain diagnosis of malaria, at all events suggests it, even in the absence of the hæmatozoon, which is often not present in this form.

Masked paludism.—In masked paludism visceral manifestations take the place of febrile phenomena, which are almost entirely absent.

It is a form of paludism which runs its course without fever. During the period of invasion the symptoms are reduced to a minimum ; the patient only complains of headache, vague digestive disturbances, with nausea, anorexia, fatigue, slight

asthenia, and some lumbar pain, all of which he attributes to the heat and overwork.

He has already forgotten these symptoms when several weeks and even several months later he presents various non-febrile disorders, which do not in any way suggest malarial manifestations, such as disturbances of the nervous system, organs of special sense and viscera.

Anæmia is certainly the most usual manifestation of masked paludism. As its malarial origin is easily overlooked in the absence of characteristic febrile phenomena, it gradually assumes its most pronounced features, giving rise to the severest clinical and hæmatological forms. This anæmia of masked paludism assumes the type of hæmorrhagic anæmia or pernicious anæmia which we have described. It is often the prodromal stage of acute cachexia. Masked paludism may also consist of nervous phenomena only, especially of a peripheral character, or neuralgias of the type which we have described above, and manifestations of the organs of special sense, particularly the eye.

Chapter V

SECONDARY PALUDISM

Secondary paludism is characterized by the appearance of *disciplined febrile attacks*, which are also called *frank attacks* (ague fits).

We adopt the term "disciplined," because it exactly expresses the regularity of the temperature curve of the attack, which is closely connected with the biological evolution of the parasite within the organism. This evolution is one of the best established conceptions of the parasitological study of the hæmatozoon. This is the schizogonic or parthenogenetic evolution, the cycle of which is completed in forty-eight hours. It is the asexual cycle which we described above in the chapter on parasitology.

The regular succession of these evolutional cycles gives rise to typical tertian intermittent fever; but under the action of various causes (increase in resistance of the organism, or quinine treatment) it may be interrupted.

It can readily be understood that secondary paludism can only assume this disciplined character if the patient is not exposed to fresh inoculations.

It is therefore the kind of paludism met with in persons who have returned to a non-malarial

district, or one which in the case of infected countries only appears in the cold season after disappearance of the mosquitoes which propagate the virus.

It should not be forgotten, however, that some persons make their first acquaintance with malaria in its secondary period. Such is the typical history of the colonial who has his first attack on returning home, as frequently occurred among the soldiers in the army of the East. As a rule, the patients are those in whom the symptoms of the first invasion were very slight and passed unnoticed; sometimes, however, the patient on being questioned has no recollection of any malaise, and it is possible that the primary period really has no symptoms.

The ague fit being the essential element in the febrile curve of secondary paludism, we shall describe it first of all. We shall then show how these attacks may recur, and take place at longer or shorter intervals, thus giving rise to a variety of temperature curves.

Previous visceral lesions may leave sequelæ, which will appear again in this secondary period of paludism, and will be revealed by symptoms which are usually attenuated.

The ague fit.—A man who appeared to be in good health or only slightly anæmic, is suddenly seized, usually late in the forenoon, with violent shivering and malaise so that he is compelled to lie down. His teeth chatter, and he shakes from head to foot. His face is pale, his look anxious, and his eyes bright. The pulse is quick, and the

extremities cold. The temperature meanwhile has risen to 100·8°. But in about half an hour's time the patient, who had rolled himself up in his blankets to get warm, begins to feel a sensation of intolerable heat. At the same time an intense headache sets in, often accompanied by pain in the back; the skin is dry and burning. The cheeks are flushed, the patient complains of dryness of the throat and intense thirst which even iced water cannot quench. The temperature rises rapidly to 104° or above.

There is an acute feeling of discomfort, which is often accompanied by nausea and even vomiting.

This condition persists for two or three hours, and then an abundant and profuse perspiration breaks out.

The patient then experiences a sensation of well-being. He covers himself again to avoid the chilling caused by the sweating, which stops in an hour's time. The fever has then fallen below 100·8°, but the normal temperature is only reached about 10 p.m., about twelve hours after the onset of the shivering.

The patient now falls asleep, passes a good night, and the next day thinks that he is cured, although he feels a little languid. The temperature is normal, and he resumes his occupation until the onset of the next fit, which will be identical with the preceding.

A close study of the temperature taken every half hour, shows, as we have said, that at the beginning of the fit it is already 100·8° F. Then it rises suddenly to reach its acme, which is about

104° less than an hour after the onset of the fit. It remains at this high level for two and a half to three hours, and then after commencement of the sweating stage it falls to 100·8°, and slowly returns to normal, eleven to twelve hours after the onset of the fit. The ague fit, as all the text-books state, runs its complete course between two *meridians*, commencing about midday and ending before midnight.

1. Principal Types of Temperature Curves

The ague fits are generally grouped so as to constitute tertian or quartan fever,[1] each fit being separated from the following by an apyrexial interval of one day in the case of tertian fever and of two days in that of quartan fever.

But the fit may remain isolated or only take place at longer intervals, of about a week's duration. On the other hand, it may form an uninterrupted series of quotidian fits, thus constituting a quotidian intermittent. Lastly, the temperature curve in secondary paludism sometimes shows a very irregular character.

(1) **Tertian intermittent fever.** — This is the typical curve of secondary paludism: the fit takes place every two days with an interval of thirty-six hours of normal temperature. It should be noted, however, that this interval of forty-eight hours between the onset of each fit may be pro-

[1] We shall not give a description of quartan fever, which has not been found hitherto in Macedonia, and which we have only seen in persons coming from Algeria.

longed or shortened (forty-seven to forty-nine hours) according to the individual. This peculiarity, to which Italian writers have drawn attention, is of importance in determining the exact moment for administering the dose of quinine for cutting short the fit.

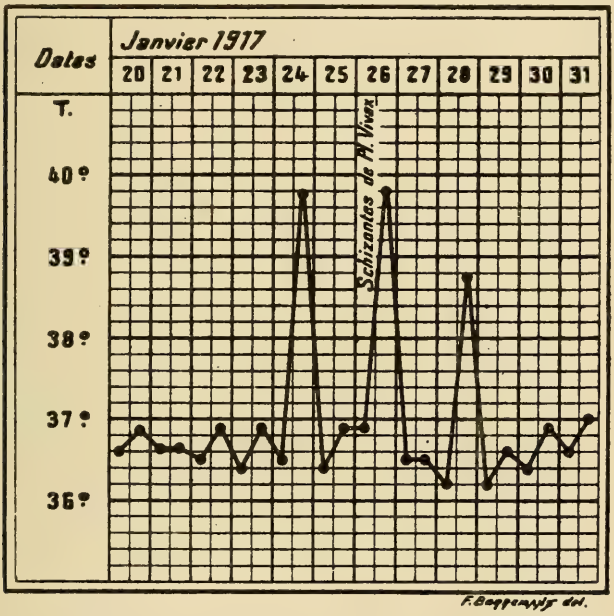

FIG. 13.—Secondary paludism. Tertian intermittent fits.

The temperature curve of tertian intermittent fever may vary considerably in length according to the progressive immunization of the organism and its resistance. The diminution in vitality of the parasite is also expressed by a diminution in the intensity of the successive fits. Lastly, quinine treatment is almost always successful in these cases.

(2) **Ague fits of septan type.**—For reasons hitherto unexplained, the fits instead of assuming the tertian type may only recur every six or seven days, even in the absence of any quinine treatment. In other cases they recur only every fortnight or every three weeks, giving rise to what has been called fits of the bi- and tri-septan type.

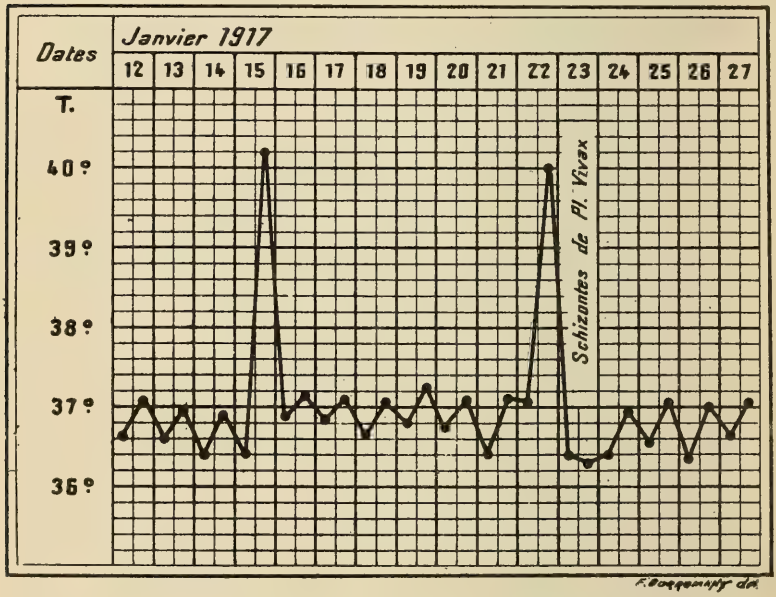

Fig. 14.—Secondary paludism. Septan fits.

(3) **Isolated fits.**—The fits may even appear to be absolutely isolated. After apyrexia for one or even two months, on the occasion of fatigue or a chill, and sometimes even without any appreciable cause there is an isolated fit which will not be repeated for a long time.

(4) **Quotidian intermittent fever.**—This is due, as Italian writers have shown, to the combination

of two tertians running their course with an interval of twenty-four hours between them. They are caused by the evolution of two generations of parasites developing at twenty-four hours' interval. There is a febrile attack every day instead of every two days, but as the first begins shortly before midday and ends before midnight, the temperature in the morning is normal, which accounts for this type of quotidian intermittent.

Irregular fever.—In some cases the temperature curve does not seem to correspond to any definite type, and its course is very irregular. But if the temperature is taken at least four times a day, it will be found that the fever really reproduces the temperature chart of a quotidian intermittent, whereas if the temperature be taken only twice a day the maximum and minimum temperatures are not indicated.

2. Clinical Syndromes

The clinical manifestations observed in the course of secondary paludism are much less frequent than in the period of relapses and second attacks of primary paludism. Their gravity is also much less. It is undoubtedly possible to meet with the same visceral syndromes as those which we described in primary paludism, but they are generally much attenuated, and in actual practice we have hardly seen more than three varieties, viz., anæmia, nervous disorders, and bilious hæmoglobinuric fever.

Anæmia.—Anæmia, which was one of the most

important visceral manifestations of the period of relapses, still remains one of the principal phenomena. But it never attains the degree of severity or assumes the pernicious character which it has during the period of a malarial epidemic. It retains, however, the same clinical and hæmatological characters, although the œdema and hæmorrhages are not often seen. A slight degree of icterus is the only phenomenon which is fairly commonly met with, its outbursts succeeding those of anæmia.

Nervous Disorders are not exceptional. They are mainly due to affection of the peripheral nerves and are neuralgic in nature. Focal lesions of the central nervous system, however, have been observed at this period and are indicated by paresis and motor aphasia; affection of the meninges is revealed by lymphocytosis and even hæmorrhage. For further details we will refer the reader to our previous description.

Bilious Hæmoglobinuric Fever [1]

Bilious hæmoglobinuric fever is fairly characteristic of secondary paludism. Though we have observed a few cases at the height of an epidemic, the affection is most frequent when the attacks show a tendency to become disciplined and when the individual is no longer exposed to fresh inoculations.

We will choose as the type for our description

[1] Armand-Delille, Paisseau, and Lemaire, *Caractères de la bilieuse hémoglobinurique chez les Paludéens de l'Armée de l'Orient. Bull. Soc. Méd. Hôp.*, June 15, 1917.

the bilious hæmoglobinuric fever which we observed in winter during the month of January.

The patient is almost always undoubtedly malarial, and is more or less anæmic in consequence. Periodically and according to a fairly regular rhythm he presents isolated febrile attacks or a series of two or three with a tertian grouping. The attack of bilious hæmoglobinuric fever generally breaks out in place of the expected ague fit on the day foreseen by the patient and his doctor.

The individual is suddenly seized with violent shivering, severe headache, and pain in the loins. He suffers from nausea and vomiting, and has the same malaise as during each of his ague fits, but in a more intense degree. The fever also rises higher than usual and exceeds 104° F. In the two or three hours following the onset of the attack, before these various symptoms have had time to subside, the patient suddenly feels a desire to urinate, and his urine is red and blood-stained. The following specimen passed is darker and of a port-wine colour. The patient is now overcome by a general feeling of lassitude and takes to his bed.

Icterus sets in a few hours after the bloody urine has been passed. It is rarely limited to the conjunctivæ, but extends all over the skin and mucous membranes, getting darker during the first twenty-four hours.

Examination of the viscera shows only a slight enlargement of the spleen which was already present before the attack, the organ just reaching the costal margin and being tender on pressure. The liver is also slightly enlarged, just reaching

below the false ribs and is also tender on pressure. The course of the affection varies, but as a rule the bilious hæmoglobinuria of the secondary period ends in recovery. The following day the patient's general condition is already improved, and he is less febrile, though he still has some anorexia, slight headache, lumbar pain, and a feeling of lassitude; on the following day the temperature returns to normal, but the attack still persists and gradually subsides in a week.

The urine on the first day is very dark and scanty, its quantity not exceeding 500-800 c.c. It is coloured red owing to a large quantity of hæmoglobin, but does not contain red cells. Its amount soon increases and returns to normal in the course of the following days.

The hæmoglobin diminishes, but the urine instead of getting clearer, becomes icteric and full of normal bile pigment. Examination of the urinary sediment after the first urine has been passed shows a few fragments of red corpuscles and when a larger amount of urine has been passed much cellular debris and even epithelial casts are found. The kidney ceases to be blocked and desquamates after having allowed the hæmoglobin to filter through.

The changes in the blood serum present a similar cycle. Examination of the blood made at the beginning of the attack shows the existence of considerable hæmoglobinæmia, the blood is laked, and the following day the serum becomes icteric and the free hæmoglobin disappears. The study of the globular resistance yields interesting results;

it is much diminished in the first few hours of the attack of bilious fever, the red cells become dissolved in normal saline solution, and then their number rises rapidly to normal (4·2 per 1000). But the patient is very anæmic. It is not uncommon to see him lose a million red cells in the course of an attack.

The affection may present two different modes of evolution. When it is to end in recovery, which occurs in most of the cases in secondary paludism, the urine becomes clear, its amount increases, the fever falls, and all the discomfort progressively subsides; the icterus disappears in a few days. The patient remains anæmic. In some cases the attack of hæmoglobinuria may recur after a period of twenty-four or forty-eight hours in which the urine remains clear. The temperature rises again and the patient again has urine of a port-wine colour, but the second attack is generally shorter and convalescence becomes rapidly established.

In fatal cases of bilious hæmoglobinuria death is due to anæmia. After the second or third day there is suppression of urine and the patient develops uræmic coma or more frequently a gastro-intestinal form of uræmia, which may last for a week. This severe course is rare during the secondary period of paludism, and is much more frequent during the height of a malarial epidemic from July to September. This form, which belongs to the period of relapses of paludism, presents a more severe course, and severer functional symptoms. Examination of the blood shows that it is as rich in parasites as during an ague fit.

Chapter VI

ASSOCIATION WITH OTHER INFECTIONS

Various infectious diseases may occur in the course of primary and secondary paludism, especially typhoid fever, paratyphoid fevers, bacillary and anæmic dysentery, and recurrent fever.

Typhoid fever.—The subjects in our field of observation had generally been vaccinated against typhoid and paratyphoid fevers, and on that account association of malaria with other dieases was rarely observed. In the cases in which the co-existence of these diseases was proved by bacteriological examination (positive typhoid blood culture with presence of hæmatozoa in the smears), the temperature curve and the course of the disease were dominated by the more powerful infective agent, in this case the hæmatozoon.[1]

In non-vaccinated cases, on the contrary, the clinical appearances in this association of diseases were those of enteric fever.

Dysentery.—Bacillary or amœbic dysentery occurring in a malarial subject aggravates his case, causes a return of the febrile attacks and predisposes to chronic intestinal lesions and malarial cachexia of the secondary period of paludism. We would

[1] Armand-Delille, Paisseau, and Lemaire, *Paludisme de 1re invasion en Macédoine. Bull. Soc. Méd. Hóp.*, March 3, 1916.

emphasize the necessity of a simultaneous examination for both parasites, hæmatozoa and amœbæ, in the blood and the stools, in view of the possibility of a dysenteriform enteritis of purely malarial origin; we have, indeed, seen cases of true dysentery which bacteriological and parasitological examination carried out under the most favourable conditions proved to be connected neither with amœbiasis nor bacillary dysentery, but which occurred paroxysmally in malarial patients whose blood was infected by the hæmatozoon.

Recurrent fever.—An association of malaria with recurrent fever may possibly take place.[1] The manifestations of secondary paludism being observed in Macedonia in the winter and spring, it is easy to understand its co-existence with this affection which is so frequent in the cold season. Paludism has no influence on its course, but we have, on the other hand, frequently seen malarial patients have tertian fits in the days following the relapse of recurrent fever.

[1] Armand-Delille, Gassin, and Lemaire, *Caractères de la fièvre récurrente observée à l'Armée de l'Orient. Bull. Soc. Méd. Hôp.*, June 15, 1917.

Chapter VII

PARASITOLOGICAL DIAGNOSIS

We shall naturally confine ourselves to a description of the essential requirements for diagnosis, and shall only mention the technique which can be carried out in the most rudimentary laboratory.

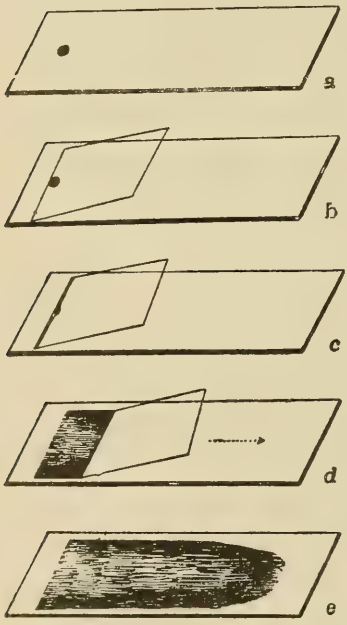

Fig. 15.—Method of making a blood film (after Langeron).

The examination for the hæmatozoa of malaria is made on *dried and stained blood films*. It is important to realize that this examination must be a very careful one; on the one hand, the proportion of positive results does not exceed 40 per cent., especially in subjects on preventive quinine treatment, while, on the other hand, with certain exceptions which we shall mention later, the number of circulating parasites is unusually small. The blood intended for examination should be taken either from the lobe of the ear or the dorsal

surface of the finger near the matrix of the nail; the skin of these regions should be very carefully wiped, as the mixture of sweat with the blood gives very bad preparations. The part should be pricked with a pin which has been passed through the flame and a very minute droplet of blood should be squeezed out, collected on a very clean slide near one of its extremities, then spread out either by a sterilized slide or a visiting card, in a very fine film, and lastly dried by waving it rapidly to and fro. After having carefully wiped the region which has been pricked a second droplet of blood should be collected, spread out and dried in the same way; except when there are special indications two good slides are sufficient each time the blood is taken.[1]

As soon as the slides are dry they should be wrapped up in paper to keep them from flies, which are very fond of blood and can completely change and spoil a preparation by repeatedly sucking it. The patient's name and any clinical notes of interest should be written on the wrapper. All the methods of staining at present in use are improvements on the processes of Laveran or Romanowski.

The preparations are easily stained *by Tribondeau's method*, provided the recommendations are strictly adhered to, which the writer took care to transcribe on the notice accompanying the bottle containing the stain. It runs as follows :—

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[1] *v.* p. 95, for the technique of the so-called "thick drop process."

Directions for using Tribondeau's Bi-eosinate.[1]

" Use carefully cleaned slides for preparing the films ; spread the blood (or organic fluid) in a thin layer over the right two-thirds of one surface by ' the visiting-card process ' by choice. Dry by shaking in the air. Do not use heat or any fixative. Mark off the smear on the left by a line with a pencil for writing on glass.

" The bi-eosinate is both a fixative and a stain.

" For fixing, drop 0·2 c.c. of bi-eosinate (about twelve drops) on the smear with a special pipette reserved for this stain. Place the slide flat on the table, cover it with a half of a Petri's capsule to avoid, especially in summer, too great an evaporation of the alcohol, which would cause immediate precipitation of the stain on addition of water, and then leave for two or three minutes.

" For staining, hold the slide slightly inclined, so as to collect the bi-eosinate on one of the long margins, add 0·6 c.c. of distilled water (about twelve drops) to the stain, mix the two fluids together all over the surface to be stained by a few rolling movements. Then put the slide down at once and don't touch it until the staining is complete, for moving it might hasten the formation of a precipitate which would spoil the result. Average time required for staining : blood, eight to twelve

[1] Avoid the use of any trace of acid or base (as in neutral stains). Mount without a cover-slip. In case of a fine precipitate spoiling a permanent preparation, it can *rapidly* be removed with 80 per cent. alcohol, and the coloration restored by pouring very dilute bi-eosinate on the slide (0·1 c c. to 2 c.c. of distilled water).

minutes; syphilitic products, twenty to twenty-five minutes.

"Finally, wash under a jet of distilled water, without first employing the staining fluid, so as to avoid fixation of the surface film on the preparation. Shake the drops off, and dry rapidly with cautious use of a flame."

Borax-eosin-blue stain.—We warmly recommend the method invented by Senevet, which yields uniformly good results, and possesses the great advantage of requiring only the ordinary reagents, methylene blue and eosin.

The following details of this excellent method, will, we think, be of some assistance to laboratory workers :—

1. Prepare the two solutions A and B.

A. Methylene blue, 1 part.
Sodium borate, 3 parts.
Distilled water, 100 parts.

Leave in the incubator for a week to a fortnight, or three weeks, at the ordinary temperature.

B. Eosin in water, 1 part.
Distilled water, 100 parts.

Ready for use.

Fix the films in 90 per cent. alcohol, or better still in absolute alcohol for at least five minutes, and after complete desiccation of the alcohol, place them face downwards on some horizontal supports (Petri's capsule, test tubes, etc.).

Prepare the following solution in a very clean glass :—

Distilled water, 20 c.c.
Solution B, 1 drop.

Mix well, then add

Solution A (methylene blue), 1-2 drops.

Mix well, and pour at once on the films. About 1-2 c.c. per film are needed.

Stain for 2-3 hours, wash rapidly under the tap, dry, and examine.

N.B.—It is best always to have a fresh solution of methylene blue, so as not to run short, if the ordinary solution is exhausted or has lost its staining capacity.

Always use the same pipettes for measuring the drops of eosin and methylene blue, otherwise the proportions would be too variable.

It sometimes happens that after having yielded excellent results for some time the methylene blue solution stains the protoplasm of the hæmatozoa too faintly. Two remedies are available: 1. Use a fresher solution. 2. Substitute some drops of a fresh solution for some of the old solution.

Make sure first of all that the failure is not due to the acidity of the water employed.

Important Note.—It very frequently happens that so-called distilled water contains more or less strong traces of acid. This acidity of the water is the cause of failure, or of a change in the stain.

To avoid this accident, use water which is absolutely neutral or even by preference very slightly alkaline. Various processes are to be recommended for this :—

(*a*) Boil the distilled water in a glass flask.

(*b*) Use rain water or melted snow.

(*c*) Add drop by drop to the distilled water, increasing quantities of a 5 per cent. solution

of borate of soda, or a 1 per cent. solution of carbonate of potash, until good results are obtained (an excess of alkalinity has the drawback of injuring the structure of certain elements, especially the nuclei of the leucocytes).

The best method for deciding whether distilled water is absolutely neutral is that described by Langeron, who uses as a reagent the alcoholic solution of hæmatoxylin: add two drops of a 1 per cent. alcoholic solution to 10 c.c. of the water to be tested, and add drop by drop a solution of 1 per cent. sodium carbonate until in five minutes' time the water becomes of a faint but definite violet colour.

(*d*) Try the ordinary water available and which sometimes gives excellent results. If the staining is successful, the following results should be obtained.

1. *Faint staining*, a drop of methylene blue (dark violet colour of the stain).

The blood corpuscles are stained pale pink or red. The nuclei of the leucocytes are violet. The neutrophils show very fine granulations of a violet colour. Those of the eosinophils are of the same colour as the red cells, sometimes even of a lighter pink. The protoplasm of the mononuclears is pale blue, and that of the lymphocytes dark blue. The hæmatozoa are very distinct owing to their purple nucleolus and pale blue protoplasm. The forms of division of benign tertian have a darker protoplasm and more intensely coloured nucleoli.

In the sexual forms the grains of pigment are very clearly seen, as well as the more diffuse and as a rule less highly stained nucleolus.

Schüffner's dots, which are sometimes fine and distinct in the medium-sized forms, are more distinct in the sexual forms (gametes).

2. *With deep staining.* With two drops of methylene blue (blue violet colour) the red corpuscles appear copper-coloured or lilac. At the same time all the staining already described is much more intense, especially as regards the nucleolus, the protoplasm of the hæmatozoa, and Schüffner's dots, which are found in some successful preparations, even in the corpuscles invaded by schizonts.

The last stain, although less pleasant to look at on account of the coppery appearance of the red corpuscles, is nevertheless to be recommended for examining the hæmatozoa, their discovery being greatly facilitated by the intensity with which they are stained.

Intermediate staining may be obtained by varying the proportions of the methylene blue and the eosin, *e.g.* by mixing three drops of methylene blue with two drops of eosin.

Laveran's panchrome. — Laveran's panchrome may also be recommended, as it gives excellent results, but we have not personally had occasion to use it.[1]

We may also mention that these methods admirably stain the spirilla of Obermeyer, and the diagnosis of recurrent fever can easily be made on a slide intended for examination of the hæmatozoa.

The examination of the blood films enables the

[1] *v.* p. 95, for the technique of this method.

three hæmatozoa of malaria to be distinguished from one another, viz.: the *Plasmodium vivax*, or agent of benign tertian; the *Plasmodium precox* or *falciparum*, the agent of so-called tropical fever or malignant tertian; and the *Plasmodium malariæ*, the agent of quartan fever. Sometimes two of these parasites will be found to be associated. We will now describe their distinctive characters.

Diagnostic Characters of Hæmatozoa

1. Plasmodium vivax

The *Plasmodium vivax* is the parasite most frequently met with during the cold season (from December to June); in summer, on the contrary, it was found in less than 20 per cent. of the cases. It is recognized by the following characters :—

(*a*) The blood corpuscle invaded is usually the seat of three important changes: it is increased in size, decolorized, and sprinkled over with small violet-red granulations known as Schüffner's dots.

(*b*) The *parasite itself* appears in four different aspects, according as it is young (schizont), adult (amœboid body), in course of schizogonic division (rosette body), or in the state of a gamete (macro- and microgametocytes). Specimens of each of these stages are frequently found in the same preparation.

(*c*) *The schizont*, a young form of the plasmodium, appears in the form of a small ring generally ovoid rather than rounded. At the narrowest pole, a small mass of violet red represents the nucleus,

EXPLANATION OF PLATE

PLASMODIUM VIVAX (Var. tertiana Laveran).

1. *Young schizont* (sporozoite just penetrating the corpuscle).
2. *Schizont.*
3. *Amœboid body* in an enlarged corpuscle presenting Schüffner's dots.
4. *Amœboid body* in course of segmentation in a much enlarged corpuscle.
5. *Rosette body.*
6. *Young macrogamete.*
7. *Adult macrogamete.*
8. *Microgametocyte.*

8 *bis. Macrogamete* undergoing retrogressive schizogony.

PLASMODIUM FALCIPARUM (Var. parva-Laveran).

9. *Sporozoite* attached to a corpuscle.
10. *Two schizonts* inside a corpuscle.
11. *Schizont* in a corpuscle presenting Maurer's dots.
12. *Three schizonts* in a corpuscle with Maurer's dots.
13. *Rosette body.*
14. *Young intracorpuscular gamete.*
15. *Adult macrogamete* (crescent type).
16. *Adult macrogamete* (microgametocyte).

16 *bis. Gamete* possibly undergoing retrogressive schizogony.

PLASMODIUM MALARIÆ (Var. quartana Laveran).

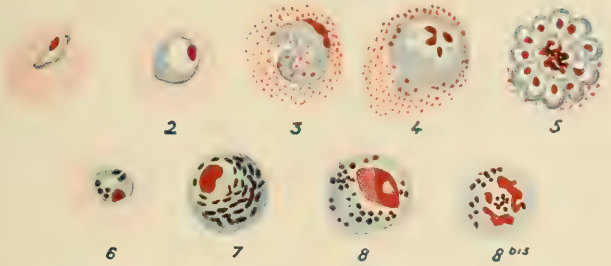
17. *Young schizont* in a non-enlarged corpuscle.
18. *More developed and pigmented schizont.*
19. *Pear-shaped schizont.*
20. *Old schizont,* much pigmented.
21. *Schizont,* undergoing segmentation.
22. *Daisy body.*
23. *Macrogamete.*
24. *Microgametocyte.*

RED CORPUSCLES (Hæmatoblasts and leucocytes).

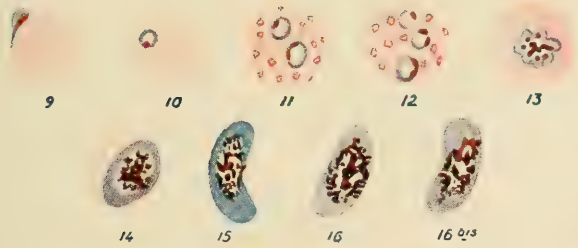
(*a*) *Red corpuscle and hæmatoblast.*
(*b*) *Hæmatoblast* in a red corpuscle simulating a schizont.
(*c*) *Red corpuscle* presenting artificial granules (precipitated colouring matter), with a hæmatoblast on its margin (cause of error).
(*d*) *Nucleated red corpuscle.*
(*e*) *Polymorphonuclear leucocytes* with neutrophil granulations.
(*f*) *Deformed mononuclear leucocytes.*
(*g*) *Melaniferous leucocytes* with some azurophil granules.

Malaria Parasites.

Tribondeau's Stain

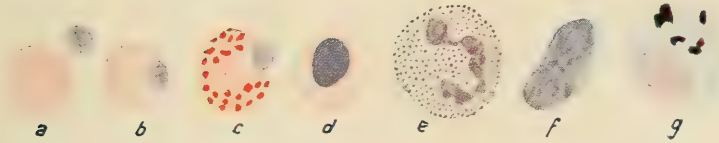


Plasmodium vivax. (var. tertiana Lav.)



Plasmodium falciparum = præcox. (var. parva Lav.)

Plasmodium malariæ. (var. quartana Lav.)



Red corpuscles. Hæmatoblasts. Leucocytes.

P. Armand – Delille, Del.

while a rounded colourless vesicle situated between this nucleus and the protoplasmic zone coloured blue, which limits the contours of the schizont, represents the nutritive vesicle.

(*d*) *The amœboid body* is merely a schizont at a more advanced stage of development. The parasite then occupies the third, the half, or two-thirds of the blood corpuscle. It is formed of two parts, one of which encloses the nucleus surrounded by a clear pink zone, the nuclear vesicle, while the other is constituted by a mass of protoplasm, containing a large nutritive vesicle ramifying in numerous slender pseudopodia, the arrangement of which varies. In these forms (large forms) the pigment is abundant and is disseminated in the protoplasm. Schüffner's dots are numerous.

(*e*) *The rosette body*, when well formed, appears as a rounded mass, filling the whole corpuscle and roughly resembling a daisy. It is constituted by the agglomeration of 16-20 merozoites, set close together round a mass of central pigment. Each merozoite consists of a large nucleus surrounded by a thin zone of protoplasm.

Side by side with the typical rosette bodies, less advanced divisional forms are to be found, intermediate between the preceding and the amœboid bodies from which they are derived. The parasite is rounded as if it were contracted, its protoplasm stains a deeper blue, the pigment is spread out into wavy lines, the nucleus is divided into two or three or more distinct portions, and the nutrient vesicle has disappeared.

(*f*) The *gametes*, or more strictly speaking the

gametocytes (for the transformation into sexual elements will only take place in the alimentary canal of the mosquito), are easily recognizable. Some which are in process of formation (young gametocytes) are still enclosed in the corpuscles, while the others which are mature are free in the blood.

The young gametocytes which are still enclosed in the corpuscles are ovoid or polygonal; their nucleolus is very large but of loose structure; the protoplasm is deeply coloured and does not show a nutritive vacuole, but contains numerous elongated pigment granules. The mature gametocytes are big rounded elements, twice as large as a red corpuscle. Their nucleus is of considerable size; their protoplasm contains numerous pigment granules arranged like needles. The macrogametocytes or future female elements can be differentiated by their nucleus being rounded and presenting a granular structure and the pigment being uniformly distributed over the protoplasm. The pigment often predominates round the nucleus; the protoplasm is more faintly stained.

It is important to realize that :—

1. The *Plasmodium vivax* is almost constantly found in the peripheral blood during the febrile attacks and generally in large quantities. 2. In the intervals it is still frequently present. 3. Although the parasitic forms found are, generally speaking, different according to the stage of the attack (the rosette body during the attack, and the schizont and amœboid body before it), and the gamete during prolonged periods of apyrexia,

as a rule a mixture of all the forms will be found in various proportions in the same preparation.

2. Plasmodium falciparum (Precox)

The *Plasmodium falciparum* is essentially a parasite of the hæmatopoietic organs ; its presence in the peripheral blood is far from constant, even during the febrile attacks (35-40 per cent. of the cases) ; as a general rule it is found in very small numbers in the blood. The preparations must therefore be examined for a long time before concluding that the hæmatozoon is absent.

The parasitic forms found in the blood differ completely according as the patient is suffering from an ordinary febrile attack or a pernicious one.

A. *In the course of the ordinary forms of tropical paludism* the forms met with in the blood belong to two types only ; the schizont and the gamete. During the febrile attacks either the schizonts are found alone or the schizonts and gametes simultaneously ; in the interval between the attacks only the gametes are found. The appearance of schizonts at this period should indicate that a relapse is imminent.

(*a*) The *schizont* of *Plasmodium falciparum* is to be recognized by the following characters : The corpuscle which it invades is not enlarged, it is not decolorized, but on the contrary often shows a slight overstaining (copper tint) ; it does not contain Schüffner's dots. The larger and irregular granulations described by Maurer often seem to be absent or at least only to be brought into view by

special stains. The parasite itself often appears in the form of a small ring, consisting of a very thin band of protoplasm and surrounding an achromatic zone; at one point the ring is occupied by a grain of chromatin stained a bright red and constituting the karyosome. Frequently this nucleus is double, each grain being connected with the other by a very thin filament of chromatin. The absence of any pigment in the schizonts of *Plasmodium falciparum* is the rule.

(*b*) The *gametes* have a characteristic form. They are the *crescents*. They are constituted by a membrane with a double wall, fairly visible protoplasm and pigment. The latter is sometimes grouped in the centre of the crescent forming a mass which masks the nucleus (macrogametocytes), or on the contrary disseminated irregularly throughout the extent of the element; the nuclear chromatin is then visible in the form of filaments (microgametocytes).

Side by side with non-pigmented schizonts which predominate and sometimes infest in large numbers the same corpuscle, and the crescents which are often present, we may also find: 1. pigmented schizonts of a larger size than the preceding; 2. rosette bodies generally with fourteen merozoites; 3. bodies which occupy an intermediate position between the schizonts and the rosette bodies, or between the schizonts and the gametocytes; they are rounded elements with deeply staining protoplasm, and a large double nucleus enclosing several thick grains of pigment.

3. Plasmodium malariæ

The *Plasmodium malariæ*, the agent of quartan fever, is quite exceptional. It is usually found fairly easily in the blood, either during the ague fits or in the interval. As in the case of *Plasmodium vivax*, the forms found in the same preparation usually belong to different stages of evolution.

The corpuscles invaded are not increased in size ; they are not decolorized and do not contain granulations. The parasite appears in the following forms, all of which possess the common feature of being clearly visible owing to *the intensity of the staining* of the *Plasmodium malariæ* which can be stained much more readily than the other hæmatozoa.

(*a*) The young *schizonts* are annular with a thick crown of protoplasm and pigmented. Subsequently they become elongated in the form of a thong, a narrow band, or a pear. Their outlines are very definite, the nucleolus is large and elongated, and the protoplasm dark blue.

(*b*) *The amœboid bodies* are quadrangular in the form of a rectangular body. The nucleolus is usually elongated, the protoplasm contains abundant pigment in the form of large granules, which frequently have a linear distribution, forming a border round the parasite. The slanting quadrangular form is not constant, for some forms are rounded.

(*c*) *The rosette bodies* formed of 6-12 merozoites show a remarkable regularity resembling a daisy in appearance.

	Plasmodium Vivax.	Plasmodium Falciparum.	Plasmodium Malariæ.
Infected corpuscle—			
Size	Enlarged	Normal	Normal
Coloration	Discoloured	Not discoloured	Not discoloured
Granulations	Schüffner's dots	Maurer's dots	Absent
Frequency of blood infection	In 80 per cent. of the cases numerous parasites	In 35 to 40 per cent. the parasites are rare except in pernicious attacks	In 80 per cent. the parasites are rather rare
Evolutional Varieties—			
Schizonts	Chiefly ovoid, protoplasm in fairly thick crown	Rounded, protoplasm in very thin crown	Elongated with very clear outlines
Amœboid bodies	Frequent in the blood, very polymorphous	Absent	Quadrangular
Rosette bodies	Mulberry-shaped with 16 or 20 merozoites	Absent except in pernicious attacks, 8 to 14 merozoites	Daisy form, 6 to 12 merozoites
Gametes	Rounded, larger than a normal corpuscle	Crescent shaped	Rounded. Size of a normal corpuscle
Parasitic formula of the ague fit	Frequent presence of all the forms	Schizonts alone or with crescents Schizonts, rosettes, crescents, and all intermediary forms in the pernicious attacks	Frequent presence of all forms

(*d*) *The gametocytes* are ovoid, richly pigmented, and contain a large nucleus. The macrogametocytes have a much darker protoplasm than that of the microgametocytes. The following table shows the various differential characters of the three plasmodia of malaria.

The examination of a specimen of blood should mean more than a search for the parasites of malaria. It is advisable also to investigate two hæmatological signs, the presence of which is important and serves as a guide to diagnosis in the absence of the parasites. These two signs are: 1. *mononucleosis*, which is especially frequent at the end of an ague fit or in the interval between two fits; 2. the presence of *melaniferous leucocytes*, which is not found till late and requires careful investigation, as the number of melaniferous leucocytes is limited.

The Thick Drop Process. If it is desirable to make a rapid examination for rare elements, especially crescents, the "thick drop process," advocated by Leishman, can be employed with advantage. Put 3-5 droplets of blood on the slide without making a film of them, but leave them to spread out spontaneously with a diameter of about 5 millimetres. Dry, then hæmolyze the preparation in distilled water; the red cells become dissolved, while the leucocytes and parasites remain intact. Dry again, and stain by one of the methods indicated below.

The elements are generally less finely differentiated, and the schizonts are less definite in outline, but a trained eye can easily recognize them among more or less well-stained leucocytes. The process enables a few parasites to be found readily in a relatively larger quantity of blood.

Laveran's Panchrome Stain.—Technique: Do not fix the smear. Spread the undiluted panchrome over the slide to be

stained. Cover the slide to prevent evaporation. Leave three minutes for fixation ; then turn the slide over, with the surface to be stained downwards, in a capsule (Laveran's or Petri's), containing the quantity of distilled water corresponding to the quantity of panchrome used. Shake at once, so as to get a good mixture. Leave for fifteen to twenty minutes according to the elements to be stained. Wash in plenty of water. Dry between two cigarette papers. Never use heat for drying.

The panchrome may be more diluted, in which case the time of staining should be prolonged. The staining, for instance, may take twelve hours (a whole night), in a 5 per cent. solution, but in that case, the preparation must first be fixed ten minutes in absolute alcohol.

It is essential that the distilled water should be absolutely neutral.

Chapter VIII

TREATMENT [1]

The various forms of treatment for malaria differ according as the disease is primary or secondary.

I. Primary Paludism

Generally speaking, whatever the clinical forms assumed by the febrile attacks, the irregular succession of which constitutes primary paludism, *the principal feature of the treatment at this time should be the energetic administration of quinine.*

The medical officer should realize that summer malaria in Macedonia is a formidable disease, against which the doses of quinine usually employed elsewhere are ineffectual. Their failure is due to many causes, viz., the nature of the pathogenic agent which in more than 85 per cent. of the cases is the *Plasmodium falciparum*; the hæmatozoon, which offers the most resistance to quinine; the multiple inoculations with the parasite due to the enormous number of the Anopheles; and, lastly, the varied conditions, such as climate, fatigue, and physical overwork, which weaken the resistance of the organism.

[1] P. Abrami, *Le Paludisme primaire en Macédoine et son traitement. Presse médicale*, March 22, 1917, and *Bud. Soc. Méd. Hôp., Paris*, March 12, 1917.

The aim to be pursued in treating primary paludism is essentially different according as one is dealing with a first attack of fever (paludism in its first invasion), or, on the other hand, subsequent attacks which constitute relapses. This distinction in our opinion is all important, and it is necessary to emphasize its significance.

During the first invasion the doctor's principal aim should be to prevent the formation of gametes. These never appear before the eight or tenth day of the disease. Their presence in the organism entails two serious consequences. In the first place, they are the only forms of the parasite which are capable of propagating the hæmatozoa after absorption by the mosquito. They are, therefore, the only source of a malarial epidemic; without gametes there would be no social paludism. Secondly, those forms which are particularly resistant to quinine tend to make the disease chronic by giving rise to fresh generations of parasites, which are the source of relapses. Without gametes there would be no individual paludism. Before the formation of gametes malaria is an acute disease which can be sterilized by quinine. After the formation of gametes malaria becomes a chronic disease, the cure of which requires a very long time as a rule.

In dealing, therefore, with the treatment of primary paludism, we must discuss successively: 1. The attack in its first invasion. 2. The period of relapses.

1. **Paludism in its first invasion.**—The treatment of the attack in its first invasion should be

early and intensive; early, because the sooner the administration of quinine begins, the greater are the chances of killing the parasites before they have had time to change into gametes, and intensive, because small doses of quinine favour the development of these resisting forms.

After the patient has been given a saline purgative (30-40 gm. of sulphate of soda), repeated, if necessary, on the following days, 3 *grammes of quinine a day should be given* throughout the duration of the febrile attack.

Two questions have to be discussed from this point of view; first, that of the manner of administration of this dose; secondly, that of the time when it should be given.

(1) **Mode of administration of quinine.**—The physician has three principal modes of administration at his disposal, *ingestion*, *intramuscular injection*, and *subcutaneous injection*. As regards *intravenous injection*, it remains necessarily an exceptional process, which can only be used in certain hospitals and particularly severe cases, like pernicious attacks.[1]

Ingestion of quinine takes place either in the form of tablets, or by preference in solution (*e.g.* quinine hydrochloride 10 gm., water 400 gm., each tablespoonful containing 50 gm. of quinine). After taking the drug the patient may be given a quantity of fluid (hot tea, weak coffee, ptisan, or lemonade) to diminish the irritating action of the quinine on the digestive mucous membrane.

Ingestion should be reserved for mild cases,

[1] *v.* Carnot and De Kerdrel, *Paris médical*, December 1916.

in which gastric symptoms (vomiting) or intestinal symptoms (diarrhœa) are absent.

It is chiefly indicated during the last days of the febrile attack at the commencement of defervescence.

The doctor should make sure himself that the quinine so prescribed has really been taken. Tanret's reagent readily enables the drug to be detected in the urine.

Intramuscular or subcutaneous injection of solutions of quinine constitutes the best method of treatment of paludism in its first invasion, provided that certain strict rules are observed, the neglect of which renders the method illusory or even dangerous.

a. Choice of solutions.—The great objection to the ordinary solutions (solution of quinine and antipyrine or quinine and urethane) is that they are hypertonic from excessive concentration of quinine. Moreover, the solution of quinine and antipyrine, which contains 0·30 gm. of antipyrine to 0·50 gm. of quinine, leads to the injection of 0·80 gm. of antipyrine daily into patients with delicate kidneys and a vascular system in a state of hypotension. Owing to their hypertonic nature, the absorption of these solutions is certainly slower and less complete than when given by the gastric route; and this defect in our opinion is sufficient to condemn a method whose chief object is to lead to more rapid absorption. Lastly, each injection often gives rise to a painful inflammatory nodule, in which the quinine is retained sometimes indefinitely; on repetition of the injection the

caustic action of the quinine renders the patient liable to necroses and more or less extensive and deep-seated abscesses, which are very slow in healing after they have been incised.

Diluted solutions of quinine should be employed, so as to reduce to a minimum the caustic nature of the product and to facilitate its rapid absorption. Roux's syringe should be substituted for that of Pravaz in giving the injections. One of us has recommended the use of the following two solutions :—

1. Quinine hydrochloride, 10 gm.
   Antipyrine, 1·50 gm.
   Distilled water, 200 gm.
2. Quinine hydrochloride, 10 gm.
   Urethane, 3 gm.
   Distilled water, 200 gm.

According to the experience of the inspector-general Grall and Dr Castellani there is a real advantage in sterilizing solutions of quinine by *tyndallization*, as sterilization at 120° C. is one of the chief causes of the necroses seen after injection.

In order to check the depressing action of quinine on the cardio-vascular system we add to the above solutions before injection the contents of an ampoule of a milligramme of adrenalin to each 30 c.c. of the solution.

b. Technique.—Injection of quinine, whether intramuscular or subcutaneous, requires *most careful antiseptic precautions*. A large number of complications (abscesses and sloughing) are due to neglect of this elementary rule. The instruments (syringes and needles) should be sterilized in the

autoclave or by prolonged boiling. The needle should be at least 5 cm. long and should be sterilized after each injection. The operator's hands should be carefully washed, and the patient's skin sterilized with tincture of iodine which, it should be noted, does not act until four or five minutes after being applied.

(*a*) *Intramuscular injections.*—Intramuscular injection should only be made at the seat of election, *i.e.* in a region where the sciatic nerve cannot be injured directly or affected by inflammation. This area is limited above by the iliac crest, and below by a horizontal line passing through the upper extremity of the natal cleft.

The needle, which should be at least 5 cm. long, should be plunged by itself vertically and deeply into the body of the muscle; the injection should be given very slowly, and as soon as it is finished, the needle should be withdrawn by a single quick movement. Injections should not be repeated in regions which are the seat of nodosities or inflammatory swelling.

c. Subcutaneous injections. — A subcutaneous injection should only be given with a dilute isotonic solution of quinine.

It should only be given in the regions of election, viz., the back of the throat, the flanks, or the abdomen.

It should be given into the subcutaneous cellular tissue, as penetration of the fluid into the dermis is liable to cause necrosis. The needle, which should be at least 5 cm. long, should be thrust in separately first of all, and it is only after it has been found

to be freely movable in the cellular tissue that the syringe is fitted on and the injection is given slowly. We have no hesitation in giving the preference to subcutaneous injection ; when performed carefully, it hardly ever has any complications.

(2) **Time for administration of the quinine.**— The three grammes of quinine should be given *in two doses :* **1.50** *gm. morning and evening when intramuscular or subcutaneous injections are employed ; or in three doses* (**1** *gm. in the morning,* **1** *gm. about noon, and* **1** *gm. in the evening*), *when they are taken by mouth.*

No account of the law of the hour is taken in adopting this method. This law is inapplicable to paludism in its first invasion, as seen in Macedonia ; the biological factors which give rise to it were not found in our patients, and the pharmaco-dynamical factors which possibly justify it when the ordinary methods of treatment are in use do not hold good when isotonic solutions are employed. Each of these two points requires further consideration.

Experiments admitting of no dispute have established that quinine is most active on the merozoites which are derived from the rupture of the rosette bodies (biological conclusion). As this rupture coincides with the onset of the febrile attack, it is important that the quinine should reach its maximum concentration in the blood at this precise moment.

Investigations carried out many years ago for the purpose of establishing the cycle of the absorption of quinine proved that the absorption reached its height at the end of six hours (phar-

macodynamic conclusion). As the result of these two conclusions, the following law was established: quinine should be given from six to eight hours before the onset of the attack. This is the law of the hour.

This law is only applicable to exceptional cases. Owing to the large number of infecting bites which are usually inflicted, malarial individuals are carriers of several generations of plasmodia, which evolve simultaneously in the system, each according to its definite cycle. The result of this, as is clearly proved by examination of the blood, is that parasites of very different ages are *present in the organs and the blood at a given moment.* The law of the hour, which is applicable to cases in which only one or at most two alternating generations of parasites are present, cannot and ought not to be observed in the cases which we have to treat.

Secondly, the pharmacodynamic idea of the optimum absorption of quinine in six hours' time is perhaps true in cases of administration of the drug by mouth or of injection of *hypertonic solutions*, but it is quite wrong when subcutaneous injections of *isotonic* solutions are given. Their absorption is extremely rapid. In less than half an hour after injection the patient feels the effects of quinine intoxication, and in less than an hour the destruction of the circulating plasmodia, even of the adult forms, is obvious, as can easily be seen in patients whose blood literally swarms with parasites of all ages.

Lastly, it is impossible to take a law of the hour

into account in a disease in which the febrile attacks are characterized by continuous or subcontinuous fever without any perodicity in the evolution of the paroxysms.

II. Period of Relapses and Second Attacks

The malarial subject, in whom the abortive treatment of the first invasion has failed and who has consequently become a gamete carrier, is henceforth doomed to suffer from a chronic disease. This disease consists of a more or less close succession of febrile relapses due to the production of generations of plasmodia derived from cystic germination and separated by intervals of apyrexia. Moreover, in addition to relapses, there is the possibility of more or less frequent reinoculations. What treatment should be adopted in chronic primary paludism—

1. During the febrile relapses ?
2. During the intervals of apyrexia ?

A. **Treatment of relapses.**—The relapse should be attacked energetically by quinine. But the doctor's aim should no longer be to endeavour to produce an immediate sterilization of the system, as this can no longer be obtained in most cases. All that one can ask of quinine is that it should shorten the febrile attack, attenuate its effects, and prevent pernicious attacks by destroying as large a number as possible of generations of plasmodia. The cure of the disease can only be obtained by successive courses of treatment, and often requires a very long time.

The treatment varies according to the character of the relapse.

1. In most cases, the relapse assumes the type of *remittent continued fever*, its duration varying from four to six, eight or ten days. The subintrant attacks which constitute it do not show any hourly periodicity, but as a rule the febrile maxima occur in the second half of the night.

(*a*) *When the fever does not reach a high level* (104° F.), and the general condition remains satisfactory; when the examination of the blood shows only a few plasmodia or remains negative, we prescribe 2 gm. of quinine (hydrochloride) daily in two doses, viz., 0·50 gm. about 8 a.m. and 1·50 gm. at about 6 p.m. Unless there is gastric intolerance, which resists ipecacuanha or sulphate of soda, the drug is given by mouth in solution or in cachets until defervescence. Otherwise we have recourse to hypodermic injections of isotonic solution. In every case adrenalin in doses of a milligramme morning and evening is associated with the specific treatment.

(*b*) *When the febrile attack is severe*, or if the examination of the blood indicates a large number of parasites, we raise the dose of quinine to 3 gm., until the temperature does not exceed 100·4° F., which occurs as a rule in two or three days. These 3 gm. are given daily subcutaneously in doses of 1·50 gm. morning and evening. We then lower the daily dose to 2 gm. given by mouth, as in the previous case.

(*c*) *Lastly, in cases of pernicious attacks*, the course to be taken differs according as we are

dealing with an algid attack or an attack of the comatose type. In the *algid attack* the danger lies not in the invasion of the parasites, which may not even be present in the blood, but in the sudden cardio-vascular collapse. In such cases the treatment urgently required is *intravenous injection of adrenalin in normal saline solution* (2 milligrammes of adrenalin in 500 to 1000 gm. of normal saline). Intravenous injection, which is the only efficacious method in subjects in whom the entire vascular system is in a state of collapse, and in whom no absorption by the subcutaneous route can be hoped for, intravenous injection, we say, has enabled us to save four out of six of our patients ; in two of them *signs of apparent death had already been present for more than five minutes ;* the injection was accompanied by artificial respiration and recovery took place. In the algid attack, therefore, treatment by quinine is of secondary importance, and need only be used after the above treatment has been instituted.

In the *comatose attack* the danger comes from the presence of the parasites in the blood. Septicæmia was a constant feature in our patients, and reached such a degree that in blood preparations it was easier to count the number of healthy corpuscles than of those infected by the *Plasmodium falciparum.* In other districts comatose attacks without infection of the blood have been repeated, as well as comatose attacks due to the *Plasmodium vivax*, but we have not personally come across such cases. All our cases were caused by the *Plasmodium falciparum*, and presented a

massive septicæmia. In such cases treatment should simultaneously combat the septicæmia by the use of quinine, and its general effects by means of revulsives, cardiac stimulants, etc. The necessity of administering quinine in such cases by injections is generally admitted; rapid action is needed. One of us, after four trials, abandoned the intravenous method, as when performed on subjects with hyperpyrexia the injection caused phenomena of shock which it seemed advisable to avoid. We make use of subcutaneous injections; 1 gm. of quinine being given on admission to hospital, 1 gm. four hours later, and another 1 gm. in another four hours. The injections are repeated in the same doses until the comatose state completely disappears; they are then reduced to two a day, each consisting of 1 gm., until recovery takes place.

2. In some cases, which are much less frequently seen, and hardly ever until the infection is of several months' duration, the relapses assume the form of *several series of quotidian attacks* separated by periods of apyrexia of variable duration. These forms generally prove very difficult to treat. It was only *by injecting* 3 *gm. a day, in two doses of* 1·50 *gm.*, and from the onset of the febrile attack, that we succeeded in reducing the number of attacks to two or three.

Of course *the management of relapses does not merely consist of treatment by quinine.* According to the predominance or association of certain symptoms, it may also be necessary to treat pulmonary, gastric, intestinal, or hepatic phenomena,

which import a special physiognomy to each febrile attack. One of the most important of these associations, both as regard prognosis and treatment, is in our opinion *dysenteriform enteritis.* Owing to its extreme prevalence during the months of September and October, its tenacity, its resistance to ordinary treatment, such as quinine, and its frequent relapses, it represented one of the most serious complications of malaria; it prolongs and aggravates the organic dissolution and leads to early cachexia. It should be combated as soon as it appears. One of us has shown in association with C. Foix that in most cases ordinary serum treatment applied early constitutes a very successful curative method. Injection of 60-80 c.c. of horse serum (anti-diphtheritic or anti-tetanic as well as anti-dysenteric serum), repeated if necessary the following day, may cause the most acute dysenteric syndromes to disappear in forty-eight hours, and reduce the stools from thirty to forty down to one or two in a day.

B. **Treatment of the intervals.**—As soon as the relapse is over *we suspend the administration of quinine* until the following relapse. The reasons which determined us to do this are numerous. First of all, quinine treatment carried out during the period of apyrexia with the object of preventing the approaching relapse invariably proved ineffective. Whatever the daily dose of quinine, its method of administration, and the duration of the cure, we never prevented the return of the attacks, but they always occurred during the course of the preventive treatment. Some of our patients

took regularly every evening 1 gm., 1·50 gm., or even 2 gm. of quinine in solution or in cachets, others were given 1·50 gm. for five days, and then after two days' interruption resumed the treatment; to others we gave 2 gm. every two days, and in others the preventive treatment was started five days before the presumed date of the return of the fever, but in every case the attempt to prevent the relapses failed.

Moreover, there seemed to us to be no doubt that *prolonged use of quinine in doses of* 1 *gm. and above presented real dangers.* Anorexia and digestive disturbances set in rapidly, and interfered with the taking of nourishment which is one of the essential elements of the treatment, while anæmia and a tendency to œdema increased with the prolongation of quinine treatment.

Lastly, relapses occurring in subjects who have been taking quinine for a long period are generally much less affected by larger doses of the drug, just as if the hæmatozoon had really acquired *resistance to quinine.*

We have, therefore, completely abandoned the administration of quinine during the intervals between the relapses. The period of apyrexia of varying duration which follows the end of a relapse, is a period of relative immunity.

Advantage should be taken of it to repair as quickly as possible the losses of the organism and to enable it to resist the following attack. Experience having shown that relapses are more frequent and severe when the patient is anæmic and exposed to fatigue and privations, rational treatment should

comprise : 1. *absolute rest* ; 2. *substantial nourishment* ; 3. *reconstitution of the blood by iron and arsenic.* An all important precaution must be added, viz., to protect the patient from fresh virulent inoculations by means of the *mosquito net.*

In those rare cases where the mechanical protection provided by the mosquito net is not available, it is obvious that *between the relapses* the malarial subject should obey the rule of preventive quinine treatment (0·50 gm.-0·75 gm. of quinine per diem).

To sum up, the treatment of chronic primary paludism comprises *a series of sterilization cures by quinine*, strictly reserved for the febrile attack, and alternating with *tonic cures to build up the system.*

The treatment of primary paludism which has become chronic, is in most cases only a palliative treatment ; it is only exceptionally that a recovery from the disease takes place in a country infested with malaria. Rapid improvement, on the other hand, takes place in healthy districts. Early repatriation of the patients is a measure the necessity of which appears to admit of no discussion.

II. Secondary Paludism

In winter and spring malaria changes in character. The febrile attacks assume the form of frank isolated paroxysms which occur with a certain periodicity, being sometimes quotidian and sometimes tertian, or septan, bi-septan, or tri-septan.

Examination of the blood at this paroxysmal period which characterizes secondary paludism reveals an inversion of the parasitic formula; preparations show that the *Plasmodium falciparum*, the predominating agent of æstivo-autumnal malaria, has been superseded by the *Plasmodium vivax*, the principal cause of the malaria of the winter and spring, a season when the disease is much less dangerous and reacts better to quinine.

We will confine ourselves to a description of the general rules of a treatment which has long been established. The treatment applies first to the ague fits, and secondly to the intervals.

1. **Treatment of the ague fits.**—The ague fit should be treated energetically, 2 *gm. of quinine* as an ordinary dose should be given in the twenty-four hours. These 2 gm. may be administered :—

(1) By intramuscular or subcutaneous injections: 1 gm. in the morning and 1 gm. at night.

(2) By ingestion (in tablets or solution), and in that case one must always make sure that the dose prescribed is really taken. The mode of administration of these 2 gm. really matters little. Some give 0·50 gm. in the morning and 1·50 gm. at night, others 1 gm. in the morning and 1 gm. at night, while others prefer fractional doses, *e.g.* 4 doses of 0·50 gm. or even 0·25 gm. eight times in the twenty-four hours.

In the case of quotidian attacks the administration of quinine should be continued regularly until the fever disappears, and in the case of tertian attacks until the disappearance of the series of

ague fits. In all cases the treatment should be continued in the same doses for at least two days after the commencement of final apyrexia.

2. **Treatment of the intervals.**—When apyrexia is established, the patient should undergo *discontinuous quininization* according to Laveran's method of successive treatments. There are various forms of this treatment; all yield the same results. The following are some of the formulæ :—

(1) *One day of quinine and one day of rest,* one day of quinine and one of rest, and so on, for six consecutive weeks. On the quinine days the drug is given in a single dose of 1 gm. or 1·50 gm. by mouth (in tablets or solution), or in two doses (0·50 gm. in the morning and 0·50 gm. or 1 gm. at night) or in four or five doses.

When an ague fit occurs in the course of treatment, the dose is raised to 2 gm. on the day of the fit and the two following days.

(2) *Job's method.*—During the first week : six days of quinine and one day's rest. During the second week : five days of quinine and two days' rest. During the third week : four days of quinine and three days' rest. During the fourth to the eighth weeks : three days of quinine and four days' rest.

On the quinine days the drug is ordered in doses of 1 gm. (a tablet of 0·25 gm. at 8 a.m., one at 10 a.m., one at noon, and one at 2 p.m.).

(3) *Carducci's method.*

1st week.

1st and 2nd day of apyrexia, 1 gm. of quinine daily.

3rd and 4th day, no quinine.
5th and 6th day, 1 gm. of quinine.
7th day, 1·50 gm. of quinine.

2nd, 3rd, 4th, 5th and 6th weeks.

8th day, 1 gm.
9th, 10th, 11th, 12th day, no quinine.
13th and 14th day, 1 gm. of quinine.

There is no need to insist on the advantage of associating with quinine treatment absolute rest, abundant nourishment, arsenic and iron.

(4) *The Italian "sterilizing" method.*—The Italian medical officers advocate the following treatment :—

1st week.

2 gm. of quinine daily.

2nd week.

One day of rest, followed by a cold bath, then 2 gm. of quinine daily.

Final cessation of quinine treatment, followed by a cold bath.

If this bath does not give rise to another ague fit, the patient is considered to be cured.

If a fresh fit occurs, the treatment must be started again.

In view of the intensity of malaria in Macedonia, Castellani and the Italian writers have recommended even 3 gm. daily during the first few days.

Ravaut's method.—Ravaut has made trial of cacodylate of soda and obtained interesting results ; but it has to be employed in large doses (20-30 cgm. daily) and, of course, combined with quinine. The

following is the method which he has had carried out in several hospitals.

A subcutaneous injection of 0·20 or 0·30 gm. of cacodylate of soda is given daily for three or four days running. The following two or four days 2 gm. of quinine in cachets are to be taken by mouth. Then the injections of cacodylate are to be resumed, and so on for at least a month, without paying any attention to the febrile attacks.

Lastly, Ravaut, in view of the signs of suprarenal insufficiency which he found almost invariably present, advocates the addition of adrenalin, which is very efficacious either in the form of injections or in the form of solution (twenty drops daily of the one in 1000 solution).

This treatment can be carried out by anyone, does not present any danger, and gives very superior results to those obtained by quinine alone.

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